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A TREATISE ON THERAPEUTICS,

COMPRISING

MATERIA MEDICA AND TOXICOLOGY,

WITH

ESPECIAL REFERENCE TO THE APPLICATION OF THE PHYSIOLOGICAL ACTION OF DRUGS TO CLINICAL MEDICINE.

BY

H. C. WOOD, M.D., LL.D.,

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D'HYGIENE, ETC.

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1887

TO

DR. GEORGE B. WOOD, LL.D.,

THIS BOOK

IS DEDICATED BY THE AUTHOR, HIS NEPHEW.

AS A TOKEN OF RESPECT AND AFFECTION.

PREFACE TO THE FIRST EDITION.

At the present time, when the shelves of private and public libraries are groaning beneath their ever-increasing loads, when a thousand presses in every city send forth day and night their printed messages until the earth is filled with them, it seems almost presumptuous for any one to offer new volumes to the world. Indeed, art is so long, life is so short, that every student has the right to demand of an author by what authority he doeth these things, and to challenge every memoir for its *raison d'être*. This being so, it assuredly will not appear egotistical for the author to state that his voluntary task was first suggested by his own wants, and that to its performance he has brought the training, labor, and experience of years spent in the laboratory, the study, the class-room, and the hospital ward.

There are a number of excellent treatises upon materia medica and therapeutics; yet in various attempts at original research, as well as in the ward and the lecture-room of the hospital, I have keenly felt the want of something more. There are many points of view from which a subject can be looked at; there are many paths by which it may be approached; and to me, other points of view, other modes of approach, have been far more enticing than those adopted in our standard treatises.

The old and tried method in therapeutics is that of empiricism, or, if the term sound harsh, of clinical experience. As stated by one of its most ardent supporters, the best possible development of this plan of investigation is to be found in a close and careful analysis of cases before and after the administration of a remedy, and, if the results be favorable, the continued use of the drug in similar cases. It is evident that this is not a new path, but a highway already worn with the eager but weary feet of the profession for two thousand years.

That very much has been thus accomplished it were folly to deny. Leaving out of sight the growth of the last two decades, almost all of the current therapeutic knowledge has been gained in this way.

Therapeutics developed in this manner cannot, however, rest upon a secure foundation. What to-day is believed is to-morrow to be cast aside, certainly has been the law of advancement, and seemingly must continue to be so. What has clinical therapeutics established permanently and indisputably? Scarcely anything beyond the primary facts that quinia will arrest an intermittent, that salts will purge, and that opium will quiet pain and lull to sleep.

To establish therapeutic facts the profession clings as with the heart and hand of one man,—clings with a desperation and unanimity whose intensity is the measure of the unsatisfied desire for something fixed. Yet with what a Babel of discordant voices does it celebrate its two thousand years of experience!

This is so well known that it seems superfluous to cite examples of the therapeutic discord; and one only shall be mentioned, namely, rheumatism. In this disease, bleeding, nitrate of potassium, quinine, mercurials, flying blisters, purgation, opium, the bromides, veratria, and a host of other remedies, all have their advocates clamorous for a hearing; and above all the tumult are to be heard the trumpet-tones of a Chambers, "Wrap your patients in blankets and let them alone."

Experience is said to be the mother of wisdom. Verily she has been in medicine rather a blind leader of the blind; and the history of medical progress is a history of men groping in the darkness, finding seeming gems of truth one after another, only in a few minutes to cast each back to the vast heap of forgotten baubles that in their day had also been mistaken for verities. In the past, there is scarcely a conceivable absurdity that men have not tested by experience and for a time found to be the thing desired; in the present, homœopathy and other similar delusions are eagerly embraced and honestly believed in by men who rest their faith upon experience.

Narrowing our gaze to the regular profession and to a few decades, what do we see? Experience teaching that not to bleed a man suffering from pneumonia is to consign him to an unopened grave, and experience teaching that to bleed a man suffering from pneumonia is to consign him to a grave never opened by nature. Looking at the revolutions and contradictions of the past,—listening to the therapeutic Babel of the present,—is it a wonder that men should take refuge in nihilism, and, like the lotos-eaters, dream that all alike is folly,—that rest and quiet and calm are the only human fruition?

Since the profession has toiled so long and found so little, if further progress is to be made we must question the old methods and search out new ones, which haply may lead to more fruitful fields. In the ordinary affairs and business of life, when anything is to be accomplished, the effort always is to discover what is to be done, and then what are the means at command. A primary knowledge of the end to be accomplished, and a secondary acquaintance with the instruments, are a necessity for successful human effort; and until the sway of this law is acknowledged by physicians, medicine can never rise from the position of an empirical art to the dignity of applied science. Until within a comparatively recent period, it has been impossible to comply with this law. But, through the advances made by the pathologists and by the students of the natural history of disease, we are fast learning the methods in which nature brings the body back to health. When this is done,—when disease is thoroughly understood,—we shall have wrought out the first element of the problem, shall have complied with the first requirement of the law.

It is scarcely within the province of the therapeutist, and certainly is not possible within the scope and limits of this work, to discuss at length the natural history of disease; but it is allowable to point out evident indications for relief; and this I have done to a greater or less extent throughout the book.

The work of the therapeutist is chiefly with the second portion of the law. Evidently, it is his especial province to find out what are the means at command, what the individual drugs in use do when put into a human system. It is seemingly self-evident that the physiological action of a remedy can never be made out by a study of its use in disease. Under all circumstances, the problem is one of the most complex with which the human mind has to grapple; and to introduce into this problem the new and ever-varying factors of the effect of disease and its natural vibrations on the system is to put the matter beyond human prescience.

In spite, then, of Dr. Niemeyer's assertion, that experiments made with medicaments upon the lower animals or upon healthy human beings have, as yet, been of no direct service to our means of treating disease, and that a continuation of such experiments gives no prospect of such service, it is certain that in these experiments is the only rational scientific groundwork for the treatment of disease. We must discover what influence a drug exerts when put into the body of a patient before we can use it rationally; and we can gain this coveted knowledge only in the method indicated.

It has been strenuously objected, especially to experiments upon animals, that drugs do not act upon the lower creatures in the same manner as they do upon man. When I first commenced the studies whose outcome is the present volume, I was profoundly impressed with the truth of this oft-repeated assertion and with the difficulties which it put in the way. To-day I do not believe that, stated in its broad sense, it is true. Indeed, more strongly, I assert that it is not true; that, in the vast majority of cases, the actions of drugs upon man and upon the lower animals are, though seemingly different, in reality similar; that the more knowledge we acquire, the fewer exceptions remain unexplained; and that the whole matter is in all probability subject to laws whose development will greatly aid in our explanation of various obscure clinical phenomena.

The general proofs of these assertions are sufficiently obvious, I think, in the following pages to render it unnecessary for me to dwell upon them at length here: moreover, if they be not so obvious to others as to myself, space is here wanting for a full discussion of the subject. I can only make a few general remarks, and point out some of what I believe to be the governing laws.

In the first place, degree and quality are distinct things, and should not be confounded. Yet they frequently are; and because it requires as much morphia to kill a pigeon of a pound weight as to destroy a man, we are told that medicines act differently upon man and the lower animals. Evidently the conclusion is a non-sequitur, and difference of susceptibility is no proof of difference in the mode of impression. A teaspoonful of Epsom salt may purge one man, whilst it may require ounces to affect another. Evidently there is a difference of susceptibility; but when the impression is once made it is of the same character in each case. As with man and man, so with man and the pigeon,—susceptibility is no measure or gauge of the character of the impression.

A large number of drugs—indeed, it may be said, the larger number of important drugs—exert in the system antagonistic actions. Thus, atropia stimulates the spinal cord, but destroys the conducting power of the nerve-trunks. It is evident that as one or the other of these influences predominates, will there be convulsions or paralysis. Now, if for any reason one animal be exceedingly sensitive to the spinal action of atropia, that animal will in belladonna-poisoning suffer from convulsions, whilst its fellow, which is affected chiefly by the nerve-action of the drug, will, under like circumstances, have paralysis. Here the mere clinician, with his superficial knowledge, seeing the paralyzed and the convulsed lying side by side, says, What a hopeless muddle! Poor fools, these vivisectors! they will never come to any good! In truth, the differences in symptoms in these and in many other cases simply depend upon differences in susceptibility; and the only lesson that the circumstance teaches is the importance of discovering the laws which govern these susceptibilities.

A law which governs the susceptibility to the action of drugs is, that the more highly specialized any system is, the more readily affected is it by a medicine. Thus, the cerebrum of a man is far more highly organized than that of any other animal, and consequently he is far more sensitive to the action of drugs which affect the cerebrum than are the lower forms. Again, in the frog the spinal system is especially developed,—probably, in proportion to the cerebrum, more so than in any other of the animals commonly experimented with: consequently the batrachian is excessively sensitive to remedies which, like strychnia, affect the spinal cord. In obedience to this law, we have resulting the action of opium,—an action which has been considered the strongest proof of the hopelessness of any attempt to explain the effects of drugs upon a man by experiments upon the lower animals. In man, opium causes deep stupor and general relaxation; in the frog, it causes tetanic convulsions. The explanation of these seeming inconsistencies is, however, very evident when the whole subject is looked at. Opium in all animals has a double action, one upon the cerebrum and one upon the spinal centres. In the frog, the latter being the more highly organized, the spinal action overcomes the cerebral; in man, the cerebrum being the more sensitive, stupor replaces the convulsions: yet in man convulsions sometimes occur in opium-poisoning, and in the frog the dose can be so managed as to cause stupor.

A second law which seems to hold sway over the action of drugs upon different animals is that great differences of function in a system affect its relation to drugs: thus, in a herbivorous animal the alimentary canal is very different from what it is in the carnivora, whose digestive organs in turn differ from those of man,—the omnivore. Medicines which act upon the alimentary canal are apt to vary in their effects upon different orders of animals.

Converse to the above law is that which renders systems which are little specialized similarly acted upon by drugs in different classes of animals.

Thus, the general structure and the functions of the circulatory system are very uniform among vertebrates, as is also the action of those drugs which affect chiefly the circulation: thus, aconite, or digitalis, or potash, influences in the one way the heart of the frog, of the rabbit, and of man.

There are a very few apparent exceptions to the uniformity of the action of drugs upon all animals, which seemingly contravene the laws that have been mentioned. These exceptions are so few, however, that without doubt advancing knowledge will by-and-by explain them all and show what are the laws which for the time being hold in abeyance or overcome those already stated.

An asserted fact, which has recently been brought forward as revealing the worthlessness of animal experimentation, is that some monkeys are not susceptible to the action of strychnia, whilst others are. Granting the truth of the asserted fact, it certainly is explainable. It is at least conceivable that a given species of animal may, by the gradually-acquired habit of feeding upon a substance containing a narcotic poison, acquire an insusceptibility to the influence of that poison, which shall, as it were, belong to its specific type, or, in other words, be an acquired specific character. The nervous system of the opium-eater becomes accustomed to the stimulant, and it is not impossible that a measure of the habit should be transmitted. If the Darwinian law of the gradual evolution by the survival of the fittest have any force, these curious apparent freaks of medicines in regard to their physiological action may be the result of this law, especially since it is species which are affected. It is not all monkeys that are proof against strychnia, but, as we are distinctly told, only one species of monkey; and, so far as I know, it is not all deer that are said to thrive when fed upon tobacco, but only the Virginia deer. Whether this conception be or be not a mere fancy, this much is to my mind very clear, that the few scattered exceptions ought not to outweigh the immense mass of evidence upon the other side, and that it is inconceivable that drugs, in their relations to animal organisms, differ from all other created things in not being subject to law.

In the early portion of this preface I stated that the work had grown out of a need felt by myself: that need was for a book into which should be gathered the many scattered facts in regard to the physiological action of medicine,—a book in which an attempt should be made to sift the true from the false, to reconcile seeming differences, to point out what we know and what we do not know, and to give a platform from which investigators might start forward without the necessity of being, as is so often the case, ignorant of what was already achieved, or of spending a great deal of time in a wild hunt through the almost boundless, but often scattered and inaccessible, ranges of Continental literature.

The plan of the present work has been to make the physiological action of remedies the principal point in discussion. A thoroughly scientific treatise would in each article simply show what the drug does when put into a healthy man, and afterwards point out to what diseases or morbid processes such action is able to afford relief. Unfortunately, in the great majority of cases our knowledge is not complete enough for this, and the clinical method has to be used to supplement the scientific plan.

I have added to the book a consideration of toxicology, so far as it is of interest to the physician. This has been done for several reasons. First, it was necessary to study the action of poisonous drugs upon man, in order to make out their physiological action; secondly, physicians are constantly required to diagnose and to treat cases of poisoning; thirdly, it is often of the greatest importance for a medical man in a court of law to be able to state what are the symptoms and post-mortem appearances produced by a given poison, what diseases they simulate, and how far and in what they differ from the phenomena of these diseases. That part of the science of toxicology which treats of the recognition of poisons in the cadaver, or in food and drink, belongs to the domain of the chemist, and I have avoided it altogether. For a similar reason, in the sections on materia medica, the chemical relations of mineral substances have not been discussed at all.

Preface to the Sixth Edition.—The rapid exhaustion of the successive editions has not only stimulated the author to render the volume, as far as lay in his power, worthy of the kind judgment and continued favor of his co-laborers, but has given him an opportunity to maintain its freshness. Comparatively few persons have a full conception of the rapid advancement of therapeutic science or the amount of labor involved in keeping up with such advance. Although only two years have elapsed since the last edition of this treatise, yet nearly four hundred papers have been studied in preparing the present one. An article upon Cocaine has been added, the chapter upon Disinfectants entirely rewritten, old literature restudied, and every endeavor made to have the book represent even more thoroughly than before the best therapeutic thoughts of the day.

TABLE OF CONTENTS.

Introduction.—Pharmacy—Therapeutics—Materia Medica—Pharmacopœia—Preparations—Effects of Medicines—Classification.

PART I.—DRUGS.

DIVISION I.—SYSTEMIC REMEDIES.

SUBDIVISION I.—GENERAL REMEDIES.

Astringents.—*Vegetable Astringents.*—Tannic Acid—Gallic Acid—Galls—Catechu—Kino—Hæmatoxylon—Rhatany—Oak Barks—Roses—Geranium—Sumach.

Mineral Astringents.—Alum—Sulphate of Aluminium—Lead and its Preparations—Bismuth and its Preparations—Oxalate of Cerium—Zinc and its Preparations—Cadmium and its Preparations—Copper and its Preparations—Silver and its Preparations.

Tonics.—*Simple Bitters.*—Quassia—Simaruba—Gentian—Nectandra—Barberry—Columbo—Boneset—Chiretta—Dogwood.

Peculiar Bitters.—Wild Cherry Bark—Cinchona—Sulphate of Quinine—Tannate of Quinine—Sulphate of Cinchonine—Sulphate of Quinidine—Dextro-Quinine—Sulphate of Cinchonidine—Chinoidine—Picric Acid—Carbazotate of Ammonium.

Aromatic Bitters.—Chamomile—Virginia Snakeroot—Cascarilla—Angustura.

True Aromatics.—Cinnamon—Cloves—Nutmeg—Allspice—Cardamom—Ginger—Black Pepper—Red Pepper—Oil of Cajeput—Eucalyptus, etc.

Mineral Tonics.—Iron and its Preparations—Sulphuric Acid—Muriatic Acid—Nitric Acid—Nitromuriatic Acid—Lactic Acid—Phosphorus.

Cardiac Stimulants.—Ammonia and its Salts—Alcohol—Brandy—Whisky—Wine—Turpentine—Digitalis—Convallaria Majalis.

Cardiac Sedatives.—Antimony and its Preparations—Veratrum Viride—Veratrum Album—Arnica—Sabadilla—Veratria—Aconite Leaves and Root—Prussic Acid—Cyanide of Potassium—Vegetable Acids.

Antispasmodics.—Musk—Castor—Valerian—Valerianic Acid—Assafetida—Camphor—Oil of Camphor—Brominated Camphor—Carbolated Camphor—Amber—Oil of Amber—Hoffman's Anodyne—Hops—Lactucarium—Black Snakeroot—Coffee, Tea, Maté, Caffein, Cocaine.

Analgesics.—Opium—Morphia—Narcein—Codeia—Narcotina—Thebaia—Papaverina—Laudania—Porphyroxia—Cryptopia—Meconia—Hydrocotarnia—Pseudomorphia—Opiania—Meconic Acid—Indian Hemp—American Hemp.

Mydriatics.—Belladonna—Atropia—Hyoscyamus—Hyoscine—Stramonium.

Anæsthetics.—Nitrous Oxide—Ether—Chloroform—Bichloride of Methyl—Bromide of Ethyl.

Excito-Motors.—Strychnia and Drugs containing it.

Depresso-Motors.—Calabar Bean—Bromide of Potassium—Bromide of Sodium—Bromide of Ammonium—Bromide of Lithium—Bromal Hydrate—Chloral—Metachloral—Chloral Camphor—Butyl Chloral—Nitrite of Amyl—Nitrite of Potassium—Nitro-Glycerine—Valerianate of Amyl—Lobelia—Gelsemium—Tobacco—Conium.

Alteratives.—Arsenic and its Preparations—Mercury and its Preparations—Iodine and its Preparations—Iodoform—Cod-Liver Oil—Phosphoric Acid and the Phosphates—Colchicum—Sarsaparilla—Guaiac—Mezereum—Sassafras—Dandelion.

SUBDIVISION II.—LOCAL REMEDIES.

Emetics.—*Vegetable Emetics.*—Ipecacuanha—Bloodroot—Apomorphia—Gillenia—Mustard—Squill.

Mineral Emetics.—Antimony—Sulphate of Zinc—Sulphate of Copper—Alum.

Cathartics.—*Laxatives.*—Foods—Tamarinds—Cassia Fistula—Magnesia—Sulphur—Potassii Sulphuretum—Sulphide of Calcium.

Purges.—Castor Oil—Mercury—Rhubarb—Goa Powder—Chrysophanic Acid—Butternut—Aloes—Senna—Euonymus—Saline Purgatives.

Drastics.—Scammony—Colocynth—Compound Cathartic Pills—Podophyllum—Elaterium—Gamboge—Croton Oil—Black Hellebore.

Diuretics.—*Hydragogue Diuretics.*—Squill—Digitalis—Broom—Sweet Spirit of Nitre.

Refrigerant Diuretics.—Potash and its Preparations—Lithium Salts—Anthydropin.

Stimulating Diuretics.—Buchu—Pareira—Uva Ursi—Pipsissewa—Juniper—Carota—Erigeron—Turpentine—Copaiba—Cubeb—Matico—Cantharides.

Diaphoretics.—*Nauseating Diaphoretics.*—*Refrigerant Diaphoretics.*—*Simple Diaphoretics.*—Jaborandi—Spirit of Mindererus—Sweet Spirit of Nitre—Alcohol—Warburg's Tincture.

Expectorants.—Atomization.

Nauseating Expectorants.—Lobelia—Ipecacuanha—Tartar Emetic.

Stimulating Expectorants.—Chloride of Ammonium—Senega—Ammoniac—Benzoin—Benzoic Acid—Balsams of Tolu and Peru—Garlic—Squill—Tar.

Emmenagogues.—*Tonic Emmenagogues.*—*Purgative Emmenagogues.*—*Stimulating Emmenagogues.*—Savine—Rue—Parsley—Apiol—Cantharides—Guaiac—Tansy.

Oxytocics.—Ergot—Cotton Root—Smut of Indian Corn.

Sialagogues.—Pellitory.

Errhines.

Epispastics.—Counter-irritation—Cantharides.

Rubefacients.—Mustard—Spices—Turpentine—Burgundy and Canada Pitch.

Escharotics.—Potash—Vienna Paste—Arsenic—Chloride of Zinc—Canquoin's Paste—Corrosive Sublimate—Acid Nitrate of Mercury—Chromic Acid—Bromine, etc.

Demulcents.—Gum Arabic—Tragacanth—Slippery Elm—Iceland Moss—Irish Moss—Liquorice Root—Sassafras—Tapioca—Arrowroot—Sago—Barley.

Emollients.—Glycerine—Poultices.

Diluents.

Protectives.—Collodium—Solution of Gutta-Percha.

DIVISION II.—NON-SYSTEMIC REMEDIES.

Antacids.—Sodium and its Preparations—Lime.

Anthelmintics.—Pinkroot—Wormseed—Koosso—Santonin—Male Fern—Pumpkin-Seed, Pomegranate, Cowhage, Kameela, etc.

Digestants.—Pepsin.

Absorbents.—Charcoal.

Disinfectants.—Lead and Iron—Corrosive Sublimate—Permanganate of Potassium—Chlorine—Chlorinated Lime—Boric Acid—Sulphurous Acid—Carbolic Acid—Salicylic Acid—Salicin—Thymol—Antipyrin—Kairin—Thallin.

PART II.—FORCES.

Caloric.—Heat: its Use in Shock, Collapse, etc.—Cold: its Local Use; its Use as a Tonic; its Use in Pyrexia.

Electricity.—General Considerations; Diagnostic Use; Use in Palsies; Use in Neuralgias; Application to Motor Apparatus; Application to Sensory Apparatus; Application to Nerve-Centres; Use as a Tonic.

APPENDIX.

The Art of Prescribing Medicines.

Tables.

A TREATISE
ON
THERAPEUTICS,
INCLUDING
MATERIA MEDICA AND TOXICOLOGY.

INTRODUCTION.

ALTHOUGH PHARMACY, or the science of preparing medicines, is entirely distinct from THERAPEUTICS, or the science of the application of medicines to the cure of disease, it is evident that some acquaintance with the former is necessary to the correct appreciation of the latter. Further, as the basis of both these studies, must first come a knowledge of MATERIA MEDICA, or the substances used as medicines. PHARMACOLOGY is the general term employed to embrace these three divisions.

In every civilized country there is some recognized official list of drugs and their preparations, known as the *Pharmacopœia*. In most places, this, being prepared with the sanction of the government, partakes of the nature of a law, but in the United States conformity to it depends upon the voluntary action of the professions of Medicine and Pharmacy, by a representative convention of which it was originally prepared and is decennially revised.

The *United States Pharmacopœia* is divided into three portions: a *primary* and a *secondary materia medica list*, and a chapter on *preparations*, with directions for their manufacture. The primary list contains medicines whose reputation is believed to be assured; the secondary list, those still on trial, or those which experience has shown to be not altogether valueless, but yet of little importance. It is evident that a knowledge of the officinal or recognized preparations, of their general mode of manufacture, and of their strength, is essential to the therapeutist. The United States Pharmacopœia recognizes twenty-nine classes of them, as follows:

DECOCTA.—*Decoctions* are made by boiling crude drugs for a greater or less time in water. It is evident that this method of preparing is ineligible when the active principle is volatile or is easily decomposed by heat, or when the drug contains much starch, whose extraction would make the preparation very thick and predispose it to rapid decomposition. The method is especially adapted to woody, hard substances, and to those containing much albumen which is coagulated by the boiling water and left in the drug.

INFUSA.—*Infusions* are made with water, either cold or hot, without boiling. They are prepared by maceration, or by displacement.

LIQUORES.—*Solutions* are preparations in which an active, *non-volatile* principle is dissolved in water.

AQUÆ.—*Waters* are solutions of *volatile* principles in water.

MISTURÆ.—*Mixtures* are preparations in which one or more medicinal substances are held in suspension in water. Of such nature are emulsions, in which some oily material is suspended by a gummy or an albuminous body.

MUCILAGINES.—*Mucilages* are solutions of gummy substances in water.

SYRUPI.—*Syrups* are sugary liquids, the menstruum or basis of which is water, with, in some cases, vinegar or alcohol.

MELLITA.—*Honeys* are preparations whose basis is honey.

ACETA.—*Vinegars* are those preparations in which vinegar, or dilute acetic acid, is used as the menstruum.

TINCTURÆ.—*Tinctures* are alcoholic solutions prepared by maceration or displacement from the crude drug, or by dissolving *non-volatile* principles. In some of them strong, in others dilute, alcohol is used.

SPIRITUS.—*Spirits* are alcoholic solutions of volatile principles, made by direct solution or by distillation from the crude drugs.

VINA.—*Wines* are preparations whose menstruum is wine.

GLYCERITA.—*Glycerites* are preparations in which glycerine is the solvent.

OLEA DESTILLATA.—*Volatile Oils* are active principles of such nature, prepared by distillation.

OLEORESINÆ.—*Oleoresins* are concentrated preparations, composed generally of a volatile oil and a resin. They are really ethereal extracts, made by the action of ether upon the crude drugs; in the case of ginger, a mixture of alcohol and ether is used.

SUCCI.—*Fresh juices* are obtained by expression of the green plant, enough alcohol being added to preserve them.

EXTRACTA.—*Solid extracts* are of two kinds; one being prepared by the evaporation of the fresh juice, the other being made in various ways from the crude drugs.

EXTRACTA FLUIDA.—*Fluid extracts* are very concentrated fluid preparations, generally so made that one minim represents one grain of the crude drug.

RESINÆ.—*Resins* are purgative resinous principles, obtained by the precipitation of saturated tinctures with water.

CONFECTIONES.—*Confections* are medicinal substances beaten up with sugar into a pasty mass.

TROCHISCI.—*Troches*, or *lozenges*, are gummy pellets or disks, so made as to dissolve slowly in the mouth.

SUPPOSITORIA.—*Suppositories* are conical bodies, prepared for introduction into the rectum, where they melt with the heat of the body. Their basis is generally cacao butter.

UNGUENTA and CERATA.—*Ointments* and *Cerates* are fatty solid preparations for external use. The cerates containing wax (*cera*) are the firmer of the two.

EMPLASTRA.—*Plasters* are solid substances spread by the aid of heat upon muslin, skin, or other similar material, and of such nature as to be adhesive at the temperature of the body.

CHARTÆ.—*Papers* are medicated leaves or sheets of paper for external use. The only officinal are those of mustard and of cantharides.

LINIMENTA.—*Liniments* are liquid preparations, generally soapy or oily, and always intended to be applied externally by rubbing.

The names of PILULÆ (*Pills*) and PULVERES (*Powders*) sufficiently indicate the character of the preparations.

The British Pharmacopœia is not divided as that of the United States, but the drugs and their preparations are arranged alphabetically.

In what way medicines produce changes in the life-actions of various parts is, and probably must ever remain, unknown, precisely as it is beyond the limit of the human intellect to know why the nerve-cell or the spermatozoon performs the prodigies of which it is capable. The fact that various substances do possess a selective tendency, so to speak, do act more forcibly on one form of tissue than on another, is, however, indisputable.

The effects of medicine are commonly divided into the *primary* and *secondary*, or the *immediate* and the *remote*. An example will probably show the difference between these in the briefest and most forcible manner. Thus, the immediate effect of a diuretic is increased urination: the secondary effect may be removal of serous effusion in some part of the body. It is evident that the latter is brought about not by the medicine itself, but by the changes it induces; the increased excretion causing a diminution of the amount of the fluid in the blood-vessels, which in turn predisposes to absorption.

The term or expression *indication* for a given remedy, being in constant use, ought to be distinctly understood; by it is meant the pointings of nature, or, in other words, the evident needs of the system. Thus, hard fæces collected in the colon are an indication for a purgative of such character as will produce watery discharges to soften them. Relaxation in a part indicates a remedy of such properties that it will awake into new life the natural contractility of the part. Again, the suppression of secretion from over-excitement, or from irritation, is an indication for some drug which will allay irritation; whilst the same suppression, when dependent upon torpor or loss of cell-activity, will call for an excitant,—an irritant. The childish absurdity of treating symptoms by any such law as "similia similibus curantur," or

" dissimilia dissimilibus curantur," is at once apparent. Symptoms are merely the surface-play of disease; and the rational therapeutist always seeks out their hidden meaning.

By far the greater number of remedies are absorbed into the blood, and thus find access to the part upon which they act. It is necessary, therefore, for them to be so placed that they can be taken into the blood-vessels.

There are five paths of entrance for medicines into the circulation,—the stomach, the cellular tissue, the rectum, the skin, the lungs. By far the most frequently employed of these is the first-named. It is evident that, in order to pass rapidly and readily into the absorbents, medicines must be in solution. When administered by the stomach, however, it is equally plain that solubility in an ordinary menstruum, such as water, is not a *sine qua non*, since the varying acidities, alkalinities, and organic contents of the alimentary juices give to them a solvent power far above that of less complex and varying fluids. Thus, a medicine insoluble in water may be dissolved by the acids of the gastric juice, while another drug may owe its activity to its solution by the alkalies or by the fatty matters of the intestinal fluids.

The dissolving power of the rectal fluids is very slight: hence, in order to act efficiently, medicines when given by the rectum must be in solution or readily soluble. Absorption, moreover, does not occur so rapidly from the rectum as from the stomach, and greater time is therefore needed to impress the system in this way. In the great majority of cases medicines are thus exhibited to obtain peculiar effects more or less local in character. Thus, an opium suppository is given in dysentery, or to quiet irritation of the genito urinary organs, or to check vomiting.

The subcutaneous tissue affords the most rapid route to the central organs. The substance must, however, always be in *perfect* solution, and not too irritating. It is thrown under the skin by means of a small syringe with a sharp hollow needle for its nozzle. Great care should be taken to avoid throwing a medicine into a vein, and so producing a sudden overwhelming effect. The point of the syringe-needle should not be thrust deeply into the tissues, but be kept just beneath the skin, and be withdrawn a little, after having been pushed along under the skin farther than necessary. The objections to the method are the danger of injecting into a vein, the slight pain of the operation, and the skill required for the latter, so that the administration cannot be left to the nurse, together with the local irritation and, it may be, inflammation, to which many drugs so used give rise. The pain may be to a great extent avoided by slightly freezing the skin by means of a spray-producer, yet, for the other reasons mentioned, the *hypodermic* method should not be employed except under certain circumstances. When, as in severe suffering, an immediate decided action is required, it is beyond all value,—the system coming under the influence of the remedy as if by magic. The dose should always be smaller than that by the mouth.

There are several ways in which medicinal principles are introduced through the skin, although the only one in common use is the application of medicated fatty preparations, either with or without friction. Absorption takes place, of course, most rapidly in those positions at which the skin is thinnest,—the inside of the thighs, the surface of the abdomen, and especially the armpits. Almost the only remedy which is introduced into the system in this way is mercury. Absorption will take place through the skin from baths, but so slowly that advantage is never taken of it in the constitutional treatment of disease,—unless the sulphur baths, sometimes employed in rheumatism, impress the general system by absorption, which seems to me doubtful. Formerly, medicines were sometimes exhibited by placing them on blistered surfaces, *beneath* the raised cuticle; but, except in the instance of morphia, so used in gastric disturbance, at present the *endermic* method is very rarely employed.

To influence the general system, the lungs are only used for the introduction of the vapors of the anæsthetics.

For *local* purposes medicines are applied to various parts,—to the skin, to the ear, nares, fauces, stomach, larynx, lungs, rectum, vagina, urethra, etc. For the last three, liquid preparations known as *injections*, or solid ones known as *suppositories*, or, in case of the urethra, as *bougies*, are employed.

For the purpose of making local applications to the respiratory organs, *atomization* is very commonly practiced. Very many forms of apparatus are in use, but the principle in all of them is the same. A rapid current of air, or of steam, is forcibly ejected from a horizontal pipe, through a capillary orifice, directly across a similar opening in a vertical tube. The rush of the vapor over this second orifice forms a vacuum; the fluid into which the base of the vertical tube is set, rushing up to fill this, is sucked or drawn out through the orifice, and as it emerges is broken into a fine spray, and is carried along by the current of air or steam into a mouth-piece, at which sits the patient. It cannot be gainsaid that in this way we are able to carry medicinal substances not merely into the larynx, but into the lungs themselves. Volatile medicines vaporized by heat are also sometimes employed in the treatment of lung affections.

There are various classes of agencies which so modify the action of drugs as to necessitate their consideration. Such are disease, climate, habit, temperament, idiosyncrasies, sex, age, time of administration, and emotions.

Disease often fortifies the system against the action of remedies, so that the dose has to be greatly increased to obtain perceptible effects. Thus, pain or delirium tremens will interfere greatly with the production of narcotism by opium; or spinal disease with purgation. Disease may altogether prevent the action of a remedy. In all these cases two rules should never be lost sight of: first, never give the medicine in such doses as would in health cause death; second, always be sure, before giving large amounts, that the remedy will not make matters worse (as a drastic in intussusception).

Climate, by giving physical habits or tendencies to the patient, often greatly influences the proper selection and dose of remedies. It is only necessary to allude to the great consumption of quinine in malarial regions as an example.

Habit—including mode of life—seems to alter, as it were, the very constitution of man. Not only does it give type to disease, by producing habitual plethora, or its opposite, but it also fortifies against the action of single remedies, or whole classes of them. Thus, in the opium-eater, a dose sufficiently large to kill an ordinary man serves only to gratify the cravings of appetite. Again, a man accustomed to one narcotic, as alcohol or opium, loses, to a greater or less degree, his susceptibility to all narcotic influence; and the patient whose bowels require daily to be moved by a cathartic finds himself react more and more slowly to medicines of that class. Again, a nervous system blunted by exposure and toil in the open air is far less susceptible to the action of remedies, and requires larger doses to influence it, than the delicate organization of a woman weakened by indolence and luxury.

Temperaments are peculiarities of organization characterizing classes of individuals; *idiosyncrasies*, peculiarities belonging to single individuals. This is scarcely the place to discuss the subject of temperaments, but it is allowable to state that while the *phlegmatic* person is no more easily moved by medicinal than by other agencies, the *nervous* individual answers as quickly to the one as to the other. Idiosyncrasies seem at present to be beyond law. They are often very remarkable, and a knowledge of them is most important for the practitioner. Thus, a relative of the author's is thrown into the most alarming fainting-fits by eating even so much butter as would be ordinarily used as a dressing for vegetables at dinner. Some persons are poisoned by the slightest touch of turpentine, others are frightfully salivated by a mere particle of a mercurial. These idiosyncrasies are numerous, cannot be foreseen, and are often very important: hence the necessity, in prescribing for an unfamiliar patient, of always asking as to his or her peculiarities.

Sex, of course, modifies all diseases connected with the organs or the process of generation, but it does more. Woman is more impressible, less robust, with less power of resisting external agencies, than is man. Consequently, the dose for her should, as a rule, be less than that for him. It is needless to remark here at length on the necessity for abstinence from strongly perturbing remedies during pregnancy or at the menstrual periods.

Age, of course, modifies materially the dose. The rule of Dr. Young, the one which seems to me the most practical and generally useful, is to add twelve to the age and divide the age by the result. Thus, a child one year old would require one-thirteenth, one three years old three-fifteenths, of the amount necessary for an adult. Other rules have been invented, but the only one which seems to me practical is the following, proposed by Dr. R. O. Cowling (*American Practitioner*, vol. i.):

"The proportionate dose for any age under adult life is represented by the number of the following birthday divided by twenty-four:" *i.e.*, for one year is $\frac{2}{24} = \frac{1}{12}$; for two years, $\frac{3}{24} = \frac{1}{8}$; for three years, $\frac{4}{24} = \frac{1}{6}$; for five years, $\frac{6}{24} = \frac{1}{4}$; for eleven years, $\frac{12}{24} = \frac{1}{2}$, etc.

Prof. Clarke (*Boston Med. and Surg. Journal*, 1872) has proposed a rule, which, although probably more accurate than either of those given, seems too cumbersome for ordinary purposes. It is based upon relative weights:

"Assuming the average weight of an adult to be one hundred and fifty pounds, for whom an appropriate dose is 1, or one drachm, the dose of most medicines must be increased or diminished in the proportion of the weight of the patient to that number of pounds. This proportion is represented by a fraction whose numerator is the patient's weight, and whose denominator is 150. If a child at birth weighs six pounds, the appropriate dose for it would be $\frac{6}{150}$, or $\frac{1}{25}$; if it weighs ten pounds, $\frac{10}{150}$, or $\frac{1}{15}$. A child two years old, weighing twenty pounds, would require $\frac{20}{150}$, or about $\frac{1}{7}$ of an adult dose; or, more precisely, $\frac{1}{7\frac{1}{2}}$. A person whose weight is two hundred pounds should have $\frac{200}{150}$, or $1\frac{1}{3}$ of an average adult dose."

It must never be lost sight of that children bear narcotics very badly, and that the doses of such remedies for them should always be proportionally smaller than for the adult.

Time of Administration.—Absorption takes place most rapidly in an empty stomach, and consequently, when rapidity of action is desired, the medicine should be given under such circumstances. Thus, a purgative acts soonest when given before breakfast. Substances which are irritating to the stomach should always be administered not only properly diluted, but also when the viscus is filled by a mass of food, which may serve still further to lessen their concentration. Hènce, such remedies as iodine and arsenic are preferably exhibited after meals. Again, some drugs, such as iron, are best dissolved by the acid gastric juice, and it is a matter of some importance to place them in the stomach after eating, when the process of digestion is most vigorous.

Mental Emotion.—Space is wanting to discuss at any length the influence of the imagination upon the action of remedies; and the reader must be referred to the delightful book of Dr. Tuke for illustration. Suffice it to state that a positive announcement that a remedy will have a certain effect has often a most remarkable influence in producing that effect, especially on persons of nervous organization and of not too great culture to have faith. I have given a hypodermic injection of a grain of morphia to a man, inducing a degree of hypnotism, and the next day, doubling the size of the injection but withdrawing all morphia, have caused a much more intense effect.

It is evident that every treatise upon pharmacology must have some plan in accordance with which the various substances treated of are arranged.*

At present, all that, in my opinion, can be reasonably demanded of any system is that it be a convenient row of pegs upon which to hang our ideas and facts, so that they may be easily retained, and be easily accessible when wanted. Under these circumstances I venture to offer, as the basis of the present treatise, without further comment, the following clinico-physiological classification, founded upon, but very different from, that of Prof. George B. Wood.

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* For a discussion of classification, see the first edition of this work.

CLASSIFICATION.

PART I.—DRUGS.

1. Substances which act on the Solids and Fluids of the Body.

a. *General Remedies.*

Class I.—Astringents.
" II.—Tonics.
" III.—Cardiac Stimulants.
" IV.—Cardiac Sedatives.
" V.—Antispasmodics.
" VI.—Analgesics.
" VII.—Mydriatics.
" VIII.—Anæsthetics.
" IX.—Excito-motors.
" X.—Depresso-motors.
" XI.—Alteratives.

b. *Local Remedies.*

Class I.—Emetics.
" II.—Cathartics.
" III.—Diuretics.
" IV.—Diaphoretics.
" V.—Expectorants.
" VI.—Emmenagogues.
" VII.—Oxytocics.
" VIII.—Sialagogues.
" IX.—Errhines.
" X.—Epispastics.
" XI.—Rubefacients.
" XII.—Escharotics.
" XIII.—Demulcents.
" XIV.—Emollients.
" XV.—Diluents.
" XVI.—Protectives.

2. Substances which act externally to the Body.

Class I.—Antacids.
" II.—Anthelmintics.
" III.—Digestants.
" IV.—Absorbents.
" V.—Disinfectants.

PART II.—REMEDIES WHICH ARE NOT DRUGS

PART I.

DRUGS.

DIVISION I.—SYSTEMIC REMEDIES.

Subdivision I.—General Remedies.

CLASS I.—ASTRINGENTS.

ASTRINGENTS are those drugs which cause contraction of living tissues That they do not act, as has been supposed, either by coagulating albumen or by calling into action the muscular function, is demonstrated by the transitoriness of their effects, and by the fact that they influence tissues containing no muscular fibre. Every living soft tissue appears to possess a normal degree of condensation, which may be departed from on either hand ; when this happens, the part is said to be relaxed in the one case, in the other to have its tonicity increased, or to be astringed. The action of astringents is always a *local one*,—*i.e.*, produced not through the intervention of the nervous system, but by direct contact with the part affected. A pure astringent should be capable of doing nothing beyond inducing contraction ; but in reality there is scarcely such a drug. All astringents are, when applied too freely, irritants; indeed, it is doubtful whether their therapeutical property of astringency is not due to the exercise of a mild form of irritation.

Our knowledge of the action of astringents upon blood-vessels is still very limited. The only published experiments are those of M. Rosenstein (*Rossbach's Pharmakolog. Untersuchungen*, Bd. ii. p. 80). He placed solutions of nitrate of silver, of acetate of lead, of sesquichloride of iron, and of tannic, gallic, and pyro-gallic acids upon the exposed mesenteric vessels of a curarized frog. The first three solutions contracted arterioles, venules, and capillaries, nitrate of silver being much the most powerful and the iron salt the weakest; the effect on the capillaries was the most permanent. The acids instead of contracting enlarged the vessels. This dilatation was not reflex, as it occurred after destruction of all of the nerve-centres. It was probably due to the irritant action of the acid.

The indications for the use of an astringent are very evident.

In the first rank among such indications is the *existence of relaxation*. Local relaxation is almost always the result of previous over-excitement. Thus, a throat is relaxed after over-use, or after inflammation.

Astringents are more efficient as local than as general remedies, but in cases of inflammation care must be taken to use them in such way that they shall not act as irritants. Applied too soon or too vigorously, they may do harm. These remarks are scarcely applicable to some of the mineral astrin gents, such as lead and nitrate of silver, which really appear to have sedative properties, and may with care be used advantageously in all stages of inflammation, whenever there is distention and relaxation of the blood-vessels, although the general action of the part be above *par*.

Closely allied to relaxation is *over-secretion*, and astringents are constantly used to *check morbid discharges*. Indeed, these discharges are often simply the result of relaxation. Thus, Asp has experimentally proven that division of the intestinal nerves and consequent paralysis and relaxation of the vessels are followed by free watery secretion. In such cases the indication for astringents is very plain. But when a morbid discharge really represents a high degree of inflammation, the same care must be practiced in the use of astringents as in treating other local inflammations. Especially is this true since free secretion is often nature's method of relieving local inflammation. Thus, when abnormal alvine discharges are dependent upon intestinal relaxation, the astringents are most valuable, but when they are dependent upon enteritis or colitis, astringents do harm.

If the morbid discharge by its profuseness endanger life, as in serous diarrhœa, astringents are urgently demanded. Very rarely, if ever, are these discharges other than paralytic in their origin ; even, however, if they be due to over-action, an astringent may be necessary to check their excessiveness.

Another indication for the use of astringents is to *check hemorrhage*, and the same general reasoning is applicable to this as to the other indications. Hemorrhage dependent upon over-action demands other treatment than by astringents. Sometimes in these cases it is necessary, however, to check the hemorrhage at all hazards, and then astringents may be used in conjunction with other measures, although they may be to some extent contra-indicated. Various astringents are employed locally to check hemorrhage due to traumatic or other ruptures of vessels. In such cases the astringents are employed as *styptics*, and do not act so much by their astringency as by coagulating the albumen of the blood, and thus forming a clot and mechanically arresting the flow.

Under certain circumstances there seems to be a general relaxation or loss of tone throughout the whole system, which may be best met by a consentaneous use of tonics and astringents.

VEGETABLE ASTRINGENTS.

The active principle of the vegetable astringents is tannic acid, and, as it is almost their sole therapeutic principle and represents them very closely, it seems proper first to consider it, and afterwards to point out any especial therapeutic virtues the crude drugs of the class may possess.

ACIDUM TANNICUM—TANNIC ACID. U.S.

There are two kinds of tannic acid, the *gallo-* and the *kino-tannic ;* of these the former yields, upon exposure to the air in a moist state, *gallic acid*, the latter a *gelatinous, inert* substance. They are further distinguished by the color of the precipitates which they yield with the persalts of iron; gallo-tannic acid producing a blue-black, kino-tannic a green-black color.

The officinal tannic acid—the gallo-tannic acid—is obtained by treating powdered galls with washed ether, which on standing separates into two strata, the upper of which is ethereal, and contains chiefly the coloring-matter and other impurities. The lower watery stratum contains the tannic acid, which is recovered by evaporation.

Commercial tannic acid is a light, feathery, *non-crystalline* powder, of a yellowish-white color, a faint odor, and an astringent, somewhat bitter taste. When absolutely pure, it is colorless and free from odor or taste other than that of astringency. Its reaction is strongly acid, and it unites freely with both organic and inorganic bases. It is very freely soluble in water, even more so in glycerine, somewhat so in dilute alcohol, scarcely at all in absolute alcohol, and not at all in ether free from water. By a heat of from 180° C. to 215° C. it is changed into *pyro-gallic acid*, which crystallizes in white, shining plates, of a bitter taste and neutral reaction. With salts of the alkaloids it produces a whitish precipitate, very soluble in acetic acid; with persalts of iron, a black (bluish or greenish) precipitate; with lime-water, a precipitate which is at first whitish, then gray, dingy greenish, and finally brownish; with gelatine or albumen, a whitish coagulum. All of these secondary products are tannates. Tannic acid also dissolves in concentrated sulphuric acid, with the production of a black color. By prolonged exposure in solution to the air, or by the action of dilute sulphuric acid, it is converted into gallic acid.

PHYSIOLOGICAL ACTION.—When applied locally to a part tannic acid is a very powerful astringent, causing contraction, and in the case of a mucous membrane, great dryness. Sometimes, when it is used very freely, its irritant influence seems to overcome its astringent action, and I have seen diarrhœa result from its administration. Several experimenters (Rosenstein, *Untersuch. Pharmakolog. Institut Würzburg*, 1875; Fikentscher, *Inaug. Dissert.*, Erlangen, 1877) have denied that it causes contraction of the blood-vessels, because when they applied it to the exposed mesentery of a "Cohnheim frog," stasis of the blood with dilatation of the vessels, not preceded by contraction, occurred. Daniels, however (*Inaug. Dissert.*, Bonn, 1864), using rabbits, obtained different results, and Lewin has shown that the method of experimentation is faulty. Clinical experience abundantly proves that tannic acid applied to relaxed mucous membranes affects their whole substance.

Tannic acid coagulates albumen with so much avidity that it has been supposed incapable of absorption, but the very elaborate investigation of Dr. Lewin cast much doubt upon the older views on this subject (*Virchow's Archiv*, lxxxi. 74). Thrown rapidly into the blood it undoubtedly causes a fatal thrombosis; but Lewin asserts that when it is injected slowly and in moderate quantities the resulting tannate of albumen is held in solution by the alkaline carbonates of the blood. He has also discovered that whilst tannin, in five per cent. solution, precipitates peptones out of watery solution, it is powerless in the presence of muriatic acid. Assuming the correctness of the investigation of Dr. Lewin, it is plain that tannic acid, when put in the stomach in small doses, must to some extent be absorbed unchanged. Dr. Lewin also asserts that it is, at least in part, eliminated unaltered, as he has frequently recovered it from the urine. At the same time it seems very probable that most of the tannic acid is converted into gallic acid, either in the stomach before absorption, or subsequently in the system, since in the viscera of a rabbit poisoned with it, Schroff (*Die Pflanzenstoffe*, Drs. Husemann, p. 1005) found only gallic acid; and according to Clarus (*Ibid.*) the greater part of ingested tannic acid can be recovered from the stools as tannate of albumen or as gallic acid. Wöhler and Frerichs have also found gallic acid with pyro-gallic acid in the urine after the exhibition of tannic acid. Whether it acts chiefly as tannic or as gallic acid, it seems after absorption to exert marked astringent powers. Lewin has shown that in frogs poisoned with it the muscles are shortened and narrowed, and when loaded stretch less and recover their original length more nearly than do normal muscles. Küchenmeister (*Arch. Physiolog. Heilk.*, 1851, 493) and Hennig (*Arch. Pharmak.*, Febr. 1853) found that in poisoned cats the spleen is notably diminished in size and increased in firmness; and Lewin has found in rabbits that it causes primary arrest of the urinary secretion, followed by a marked increase of the flow.

THERAPEUTICS.—As tannic acid undergoes in the system conversion into gallic acid, the latter is to be preferred to it when the part to be acted on can only be reached through the circulation. As a local application, tannic acid is much more powerful than gallic acid. Locally applied, it may be used to *overcome relaxation*, as in *spongy gums*, *mercurial sore mouth*, *hemorrhoids*, *chronic sore throat*. To *check hemorrhage* it may be used whenever the source of the flow can be reached directly, as in *epistaxis*, *hæmatemesis*, *hemorrhage from the bowels*, etc. To arrest *excessive secretion* it may be employed locally in *leucorrhœa*, *diarrhœa*, *old abscesses*, *chronic ulcers*, *excessive perspiration*, *osmidrosis*, and various diseases of the skin. It is also often very useful for the purpose of hardening parts exposed to friction, as in cases of *sore nipples* and *tender feet*.

TOXICOLOGY.—Tannic acid can scarcely be called poisonous; although Rollett reports the case of a young girl in whom a very large quantity of it induced severe gastric and abdominal pains, with obstinate vomiting and constipation, fever and general malaise. Both Schroff and Judell assert that eighty grains of it produce no symptoms of importance in the rabbit.

As an *antidote* it is useful in tartar emetic poisoning, forming an insoluble tannate of antimony. It is also the best chemical antidote for the poisonous alkaloids; but, as the compounds it makes with them are slowly dissolved by the fluids of the alimentary canal, it must always be followed by emetics and cathartics.

Administration.—When given to act on the stomach, as in hæmatemesis, tannic acid should be in powder (ten to twenty grains). When the bowel is to be influenced, as in diarrhœa, the drug should be administered in pill (three to five grains), so that, if possible, it may pass the pylorus undissolved. For local use a solution in glycerin may be employed, or the officinal *ointment* (*Unguentum Acidi Tannici*, U. S., 1 to 9), or the *troche* (*Trochisci Acidi Tannici*, U. S., 1 grain each).

ACIDUM GALLICUM—GALLIC ACID. U.S.

Gallic acid is a white, powdery substance, in fine acicular prisms, soluble in one hundred parts of cold water, in three parts of boiling water, and freely soluble in alcohol and ether. Its taste is acidulous and astringent.

According to the officinal method, gallic acid is prepared by the exposure of moistened powdered nut-galls in a warm place for a month. A species of fermentation, with the development of a peculiar fungus, is said to occur, during which oxygen is absorbed, carbonic acid evolved, and glucose and gallic acid are produced. M. Sacc (*Chemical News*, July 24, 1871) has recently denied this, affirming that the change is simply one of hydration, tannic acid being an anhydride of gallic acid. Tannic acid also may be rapidly converted into gallic acid by the action of dilute sulphuric acid.

Gallic acid produces with salts of the alkaloids whitish precipitates, with persalts of iron a bluish precipitate, with lime-water a whitish precipitate, changing to blue, and then to violet or purplish,—all of these precipitates being gallates. It does *not coagulate gelatine* or *albumen*, and dissolves in concentrated sulphuric acid, with production of a deep-red color. It has the power of reducing silver from its solution slowly in the cold, instantaneously if warmed. As an astringent it is similar to, but much less powerful than, tannic acid. It escapes from the body through the kidneys.

Therapeutic Action.—Gallic acid is not nearly so efficient as tannic acid when applied locally, but, because it does not coagulate albumen, should always be preferred when the part is to be reached through the medium of the circulation. It is useful as an astringent in *hæmoptysis*, *hæmaturia*, *colliquative sweats*, etc. It has been recommended in *bronchorrhœa* and in the profuse expectoration of *chronic phthisis*. In my hands, however, it has completely failed in the latter affections. In certain forms of *Bright's disease*, when there was an abnormally large secretion of highly albuminous urine, I have found it to lessen very materially the excretion of albumen.

Administration.—Gallic acid may be given in powder, or sometimes in pill form. The dose of it is from ten to thirty grains, repeated as often as may be necessary. An *ointment* (*Unguentum Acidi Gallici*, 1 to 9) is officinal.

GALLA—GALLS. U.S.

Galls are vegetable excrescences, which are produced by the deposition of the ova of insects. They occur on almost all kinds of plants, even on fungi, but the officinal gall is developed on the Quercus infectoria by the act of the fly *Cynips* (*Diplolepis*) *tinctoria.* There are in commerce two varieties of galls, derived chiefly from the Levant. The *blue* or *green galls* are globular, solid bodies, from the size of a pea to that of a hickory-nut, externally smooth, or more commonly marked with large tubercles. They are the young galls which have been gathered before the ova of the fly have hatched, or before the caterpillar has eaten out the interior of its birthplace. The *white galls* are large, light, hollow bodies, with a hole, through which the Cynips has escaped after having fed upon the interior during its whole larval life. They contain but little tannic acid, and are of comparatively little value.

THERAPEUTICS.—The sole value of galls is as the source of tannic acid. As galls, they should not be used in medicine; but the United States Pharmacopœia recognizes a *tincture* (*Tinctura Gallæ*, 1 to 5), and an *ointment* (*Unguentum Gallæ*, 1 to 9).

CATECHU—CATECHU. U.S.

An extract of the wood of an East Indian tree,—the Acacia Catechu. It occurs in masses of various shapes, or in small fragments, of a dull reddish-brown color, and having a bitterish, astringent, and, after a time, sweetish taste. It contains kino-tannic and catechuic acid. *Pale catechu*, or *gambir*, which is officinal in the British but not in the United States Pharmacopœia, occurs in small cubes, about an inch in diameter, lighter than water, pale-yellowish within, deep-yellowish or reddish-brown externally. Catechu is a powerful astringent, which may be used externally, or for *diarrhœa*, in the dose of twenty to thirty grains.

The U. S. Pharmacopœia recognizes a *compound tincture* (*Tinctura Catechu Composita*, Catechu 12, Cinnamon 8, to 100), of which the dose is one to three fluidrachms, and a *troche* (*Trochisci Catechu*, 1 grain each).

KINO—KINO. U.S.

The inspissated juice of Pterocarpus marsupium and of other plants. It occurs in small, irregular, angular, shining, reddish, brittle fragments, of a bitterish, highly astringent, and, after a time, sweetish taste. There are four varieties,—the East India, West India, Botany Bay, and African. Of these, the first is common, the second rare, and the last two are never seen in our market. Kino contains kino-tannic acid, and in its therapeutic powers is almost identical with catechu. The dose is twenty to thirty grains. A *tincture* (*Tinctura Kino*, 1 to 10) is officinal. Dose, one fluidrachm.

HÆMATOXYLON—HÆMATOXYLON. U.S.

The heart-wood of Hæmatoxylon Campechianum, or logwood-tree, a native of Central America. A dense, heavy wood, of a deep reddish-brown color, containing, besides kino-tannic acid, a crystalline principle, *Hæmatin* or *Hæmatoxylin*, which when pure is yellow, but readily yields red or purple dyes. Hæmatoxylon is a mild efficient astringent, valued on account of its sweetish taste. It is readily taken by children, but is sometimes objected to on account of the staining of the diapers by the blood-red stools which it produces. The following formula offers an efficient and elegant remedy for *diarrhœas* of relaxation; the proportions may be varied to suit individual cases: ℞ Ext. hæmatoxyli, ʒii; Acid. sulph. aromat., fʒiii; Tinct. opii camph., f℥iss; Syrupi zingiberis, q. s. ad f℥vi. M.—Dose, a tablespoonful, properly diluted. The *extract* (*Extractum Hæmatoxyli*) is officinal, dose, ten to thirty grains.

KRAMERIA—RHATANY. U.S.

The root of Krameria triandra, a native shrub of Peru. This woody root, as it occurs in our markets, varies from one-fourth inch to one inch in diameter, and from half a foot to three feet in length. The readily separable bark is of a deep-reddish color. The internal woody portion is of a lighter hue, although decidedly reddish. The bark contains a much larger percentage of the active principle, kino-tannic acid, than the wood. Rhatany is a powerful astringent, similar in virtue to kino and catechu, but is never administered in powder. The United States Pharmacopœia recognizes an *extract* (*Extractum Krameriæ*), dose, grs. v–x; a *tincture* (*Tinctura Krameriæ*, 1 gr. to 1 C.c; and a *fluid extract* (*Extractum Krameriæ Fluidum*), dose, twenty drops.

Quercus alba, U. S., and **Quercus tinctoria** are the inner barks of the trees whose names they bear,—the *white* and the *black oak* respectively. The latter is a rough, yellowish-brown bark, which is used in dyeing, under the name of *quercitron*. On account of its imparting readily its color, it is rarely, if ever, employed in medicine. White-oak bark also stains, but not nearly so deeply as does black-oak bark, and, containing largely of gallo-tannic acid, is used as a means of making cheap astringent infusions for baths, vaginal washes, etc., also in powder for poultices.

Rosa Gallica, U. S., is the dried petals of the half-opened flowers of the hundred-leaved rose. They are of a deep-red color, of a pleasant scarcely astringent taste, and contain a small percentage of gallo-tannic acid, red coloring-matter, and a trace of volatile oil. Sulphuric acid changes their infusions or tinctures to a bright-red color. They are almost destitute of therapeutic virtues, but their preparations, except the fluid extract, are used as elegant vehicles. The U. S. Pharmacopœia recognizes a *fluid extract* (*Extractum

Rosæ Fluidum), a *honey* (*Mel Rosæ*, 1 to 12.5), a *confection* (*Confectio Rosæ*), and a *syrup* (*Syrupus Rosæ*, fluid extract, 1 to 10).

Rosa Centifolia, U. S., or *Pale Rose*, contains no tannic acid, but a volatile oil, and is used simply on account of its pleasant odor; out of it are prepared *rose water* (*Aqua Rosæ*, U. S.) and the very elegant, bland emollient ointment, *cold cream* (*Unguentum Aquæ Rosæ*, U. S.).

The rhizome of Geranium maculatum Linn., an herbal plant, which grows abundantly in open woods in the middle United States, and may be recognized by its light-purplish petals, slender pointed sepals, and five-parted leaves, is officinal under the name of *Geranium*. It occurs in pieces from one to three inches long, one-quarter to one-half inch in thickness, wrinkled, contorted, tuberculated, often fibrillated, brownish externally, grayish internally. The taste is a nearly pure astringent one. It contains largely of gallic and tannic acids, and is a somewhat popular astringent, although rarely used by practitioners. It may be boiled in milk for children needing a mild astringent. Dose, grs. xx–xxx.

Rhus Glabra. U. S.—The fruit or berries of the sumach contain a very large percentage of tannic and malic acids. They are not used internally, but their fluid extract (*Extractum Rhois Glabræ Fluidum*, U. S.) affords a very superior gargle in anginose affections. It may be diluted with from two to four parts of water, and chlorate of potash added to saturation.

MINERAL ASTRINGENTS.

ALUMEN—ALUM. U.S.

Formerly the double salt of alumina and potash constituted the ordinary alum as well as the officinal drug. Ammonia as a secondary product in the manufacture of coal gas has become so cheap, however, that it is now used very largely instead of potash, although the potash alum is alone recognized in our officinal standard. The two salts are identical in physical and medical qualities, but when the ammonia alum is triturated with lime the odor of ammonia is at once evolved. Alum occurs in octahedral colorless crystals, which are often aggregated into large masses. Its taste is astringent, acidulous, and sweetish. It is soluble in about fifteen times its weight of cold and in about three-fourths its weight of boiling water. It is slightly efflorescent, and when heated a little beyond 112° Fahr. parts with its water of crystallization, and is converted into a white powder, which is officinal as *Alumen Exsiccatum*, or *Dried Alum*. The alkalies and their carbonates, lime, magnesia and its carbonate, tartrate of potassium, and acetate of lead are incompatible with alum.

Physiological Action.—As alum, even in very dilute solutions, coagulates albumen, it would appear as though it could not be absorbed. Since, however, both Drs. Geo. B. Wood and A. Stillé assert, on what authority I do not know, that alumina can be detected in the urine of persons taking it, it or its derivatives must find a way into the blood. What changes it undergoes in the alimentary canal, or in what form it enters the blood, is not known.

Applied to a tissue, it acts as a very powerful astringent and irritant. Orfila found that in dogs one or two ounces of it simply induce violent vomiting and purging, whilst in Mitscherlich's experiments two drachms of it produced in rabbits fatal gastritis, evidently on account of their inability to vomit.

In man, large doses internally produce symptoms of violent gastric irritation. One ounce and five drachms of the burnt alum caused death in a man in eight hours. (*L' Union Médicale*, No. 64, 1873.)

THERAPEUTICS.—Alum may be used locally to serve all the purposes of a very active astringent. It has been employed very frequently with success as a styptic to arrest hemorrhage; and, applied by the atomization of its saturated solution, I have found it of signal service in *hæmoptysis* and in *bronchorrhœa.* It also frequently enters into the composition of gargles for *sore throat;* but this practice is to be reprobated, since alum acts very destructively on the teeth. In *colliquative sweats*, sponging at bedtime with alum-water, or, still better, the taking of an alum-water bath, will often materially aid in restoring the lost tone to the skin. In *chronic ulcers* with exuberant spongy granulations, and in certain conditions of *conjunctivitis*, *alum curd* is often applied with benefit. When it is desired to exert an astringent action upon the internal organs, alum is not nearly so useful as other members of the class.

Owing to its irritant properties, alum when given in sufficient amount acts as a mechanical emetic, and may be used as an adjuvant to the sulphate of zinc or of copper in narcotic poisoning. Originally introduced by Dr. C. D. Meigs, it is believed to be of service in *membranous croup* not only by its emetic action, but also by modifying the mucous membranes with which it comes in contact in its passage down and up.

So long ago as the last century, Dr. Grashius, of Holland, commended alum in *colica pictonum*, and although for a long time its value was not recognized, abundant confirmative testimony has recently been brought forward. Since it is a soluble sulphate, it is of course a chemical antidote to any lead salt which may be in the alimentary canal. It is, however, of service when there is no lead in the primæ viæ, and must act in some way as yet unknown. It has, indeed, been used with asserted success in other neuroses of the alimentary canal,—in *gastralgia* and in *intestinal neuralgia.* Dr. Aldredge even commends it in *habitual constipation. Burnt alum* is used as a very mild escharotic for exuberant granulations in ulcers.

ADMINISTRATION.—As an astringent, the dose of alum is from ten to twenty grains; as an emetic, a teaspoonful of the powder for a child, a tablespoonful for an adult, in syrup, repeated in fifteen minutes; in *colica pictonum*, twenty to forty grains every three or four hours, combined with morphia.

Alum curd may be made by dissolving two drachms in a pint of milk, and straining, or by rubbing the alum with white of egg.

ALUMINII SULPHAS—SULPHATE OF ALUMINIUM ($Al_2O_3 3SO_3 + 18HO$ —$3SO_4,Al_2 + 18HO$), U.S.—This salt, which occurs as a white powder, or in lamellated cakes, or in a crystalline cake, is used externally as a powerful astringent and antiseptic. Its solution has also been employed by injection for the preservation of cadavers.

PLUMBUM—LEAD. (Pb.) U.S.

When a soluble salt of lead is applied to a part in not too concentrated solution, it acts as an astringent and sedative. Owing to the contraction of the vessels which is induced, the tissue becomes blanched, and any inflammatory action which may be present is remarkably affected. When in concentrated solution, the mildest preparations of lead are capable of acting as irritants, increasing or even originating inflammation. When the salts of lead are taken internally in therapeutic doses, no decided symptoms are generally induced, except a diminution of the secretions, especially of those of the alimentary canal. Sometimes, when full therapeutic doses are exhibited, a slight lowering of the frequency and force of the pulse (see Laidlaw's Observations, quoted by Stillé, *Therapeutics*, second edition, p. 177, vol. i.) is said to result, but I have never witnessed this. The insoluble preparations of lead act similarly but less decidedly than the soluble; yet it is doubtful whether they can under any circumstances become irritant.

TOXICOLOGY.—The salt of lead with which intentional or accidental acute poisoning is most frequently induced is the acetate.* The first result of a toxic dose of this is in most cases a persistent sweet, somewhat metallic taste; this in a few minutes is followed by vomiting, which may or may not be preceded by nausea. The matters vomited are often milky-white, from the presence of chloride of lead. A severe burning persistent pain in the abdomen now comes on, and is accompanied with a craving for drink. There may be obstinate constipation, or diarrhœa may ensue; in either case the stools are generally black from the sulphuret of lead. In certain cases a state of collapse is developed; the pulse falls to forty or fifty per minute, the voice is lost, the face is deadly pale, the lips are livid, and syncope seems imminent. In other instances the nervous symptoms may predominate, or they may accompany those of disordered circulation: cramps in the calves of the legs, severe neuralgic pains in the extremities, paralysis and anæsthesia, vertigo, stupor, may any or all of them be present. In fatal cases, coma, with or without convulsions, finally develops. A distinctive mark of lead-poisoning, which sometimes is present very early, is the blue line upon the gums. After death inflammation of the alimentary mucous membrane is sometimes, but not always, found.

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* According to Husemann (*Handbuch der Toxicologie*), the Poudre de Succession, so famous during the reign of Louis XIV., was composed chiefly of acetate of lead.

The fatal dose of sugar of lead is between one and two ounces; the subacetate of lead is even more poisonous, and the nitrate acts as a violent irritant. The carbonate appears to be incapable of causing acute poisoning.

The treatment of *acute lead-poisoning* consists in the evacuation of the stomach, if necessary, the exhibition of the sulphate of sodium or of magnesium, and the meeting of the indications as they arise. The Epsom and Glauber's salts act as chemical antidotes, by precipitating the insoluble sulphate of lead, and also, if in excess, empty the bowel of the compound formed. To allay the gastro-intestinal irritation, albuminous drinks should be given and opium freely exhibited.

Of all forms of poisoning, chronic lead-poisoning is the most common. It is almost always accidental, and occurs most frequently among those whose occupation exposes them to daily contact with some compound of the metal, manufacturers of white lead, painters, glaziers, and similar artisans furnishing the greater number of victims. It is seen, however, in persons of all conditions of life, for although neither food nor drink is often purposely adulterated with it, yet it is frequently introduced into the system accidentally along with those necessities. Lead pipes are habitually used for the conveyance of water, and when that water contains salts of lime, even in minute proportion, no evil results, because through the decomposition which ensues insoluble coatings are deposited on the inside of the pipes.* When the water is pure, no such reactions occurring, the lead is slowly dissolved in the form of a carbonate, and poisoning may result. Poisoning has also frequently resulted from the use of cosmetics and hair-dyes, from cooking bread with painted wood (*Le Progrès Méd.*, 1877, 349), from imperfectly burnt pottery (*Schmidt's Jahrbücher*, Bd. cxliv. p. 279; *Phila. Med. Times*, vol. iv. pp. 241, 483), and in other curious ways.

The most ordinary form of chronic lead-poisoning is that in which colic is the first decided symptom. After some days of malaise and wretchedness, or sometimes very suddenly, the victim is taken with abdominal colicky pains, which increase in intensity until they become very severe. They are constant, with occasional exacerbations, are sometimes dull, sometimes sharp, are generally described as twisting, and seem to centre around the umbilicus. There is very often repeated retching and vomiting. The walls of the abdomen are retracted, rigid, knotted; the bowels are obstinately costive; the tongue is contracted and whitish; the appetite gone; and the thirst sometimes excessive. Neuralgic pains in the thorax and in the extremities are of frequent occurrence. In some cases the conjunctiva is distinctly icterode.

These symptoms usually abate after a time, but are very apt to recur with increasing severity, especially among those who are habitually exposed to the cause. In one of these repeated attacks severe cerebral symptoms may come on suddenly, or after some days of headache; delirium, either mild or maniacal, or stupor, is in some such cases the chief manifestation, but epileptiform convulsions are more common, constituting the condition known as *encephalopathia saturnina*, or *saturnine cerebritis*. The convulsions are often very severe, and end in coma, in which death may take place; yet recovery may occur after the most severe symptoms (case, *Charité Annalen*, ix. 159). The nervous symptoms of lead-poisoning may be developed after the first attack of colic, or they may occur without marked abdominal disturbance. The most common of them is the local paralysis known as "*drop wrist*." This is a complete palsy of the extensor muscles of the forearm, which allows the hand to drop forward. It is often associated with complete or partial anæsthesia of the part affected, or, in some cases, of the still unparalyzed shoulders. Strabismus is sometimes present in lead-palsy, due to the paralysis of the external recti.

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* For an elaborate article on the chemical relation of water to lead, see *Schmidt's Jahrbücher*, Bd. cxliv. p. 279.

Among the rarer forms of nervous disturbance induced by lead may be mentioned—amaurosis from atrophy of the optic nerve, the atrophy being probably the result of an optic neuritis (see *Phila. Med. Times*, iv. 241; also *Berliner Klin. Wochenschr.*, 441, 1884, 370)—hemiplegia and hemianæsthesia—and violent and intractable chorea.* I have seen several cases in which the symptoms resembled those of an acute poliomyelitis, with rapid wasting of all the muscles of the arms and shoulders, the legs also being affected. In one instance the bladder and rectum were paralyzed, but the patient, long at the point of death, finally recovered. In some cases violent neuralgic pains are the chief symptoms of lead-poisoning.

In some cases of lead-poisoning the kidneys are fatally involved, although temporary albuminuria may occur without serious implication of the kidneys. On the other hand, fatal nephritis may exist when there is no albumen in the urine. (Dr. Lancéraux, *Trans. Internat. Med. Congress*, 1881, ii. 191.) A persistent low specific gravity of the urine in a saturnine patient is of very serious import. Geppert (*Ztschr. Klin. Med.*, v. p. 161) confirms the observation, previously made by Olivier, that in temporary plumbic albuminuria many isolated kidney epithelial cells may often be found in the urinary sediment, and it is evident that a persistence of this condition must end in chronic renal disease. After death, which may be induced by uræmia, the kidneys are found contracted, granular, with excessive development of the fibrous tissue (followed by contraction) and great thickening of the walls of the blood-vessels: these changes are identical with those of contracted kidney produced by gouty and other irritant poisons. As Ellenberger and Hofmeister have shown that the lead is chiefly eliminated by the kidneys, the frequency of plumbic nephritis is readily explained; but it is not readily perceived why it is so frequently associated with an arthralgia, whose course and lesions closely simulate those of chronic gout. Garrod (1859), Dickinson, Lanceraux, Rosenstein, Leyden (*Zeitschrift f. Klin. Med.*, 1884, p. 881), and other authors have reported so many cases of this association of renal and gouty manifestations, that it can scarcely be doubted that the plumbism is the cause of the gouty symptoms, and not simply a complication of gout.*

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* For discussion of details of these peculiar conditions, see Beau, *Arch. Gén.*, 1848; Manouvriez, *Arch. de Physiolog. Normal et Patholog.*, 1870, 411; 1876, p. 762; A. De Cours, *De l'Hemianæsthesia saturnine*, Paris, 1875; Proust, *Progrès Méd.*, 1879, vii. 546; Debove, *Ibid.*, 99, 117.

According to Dr. E. Levy (*Schmidt's Jahrbücher*, Bd. clii. p. 250), acute asthma is rarely produced by the inhalation of the dust of white lead, and chronic saturnine asthma is sometimes seen in feeble, narrow-chested people. The epileptiform convulsions produced by lead are in some cases secondary to chronic nephritis, but in other instances are due directly to the action of the lead (see paper of Dr. Rosenstein, *Archiv Path. Anat.*, Bd. xxxix., 1867, p. 4). Upon pregnant women the influence of the poison is very deleterious, and Dr. Constantine Paul (*Archives Générales*, vol. xv., 1860, p. 513) has shown that it very commonly produces the early death of the fœtus.

As any of these obscure manifestations of lead-poisoning may exist, and even prove fatal, without a distinct history of other more characteristic phenomena, great care is sometimes necessary to avoid being misled, and not rarely the true nature of saturnine epilepsy or of saturnine albuminuria is overlooked. Hence the importance of the *blue line upon the gums where they join the teeth*, which probably exists in a greater or less degree in all persons suffering from lead-poisoning who have teeth, although very great cleanliness may lessen it. It is said to be the result of a formation in the walls of the capillaries of the sulphide of lead. Dr. J. J. Putnam affirms, however, that he has seen several cases of obscure nervous disease, probably due to lead, in which there was no blue line upon the gums, although the metal could be detected in the urine. In looking for the metal a quart of the urine should be boiled down, as the amount of the lead is very small (*Trans. Amer. Neurolog. Assoc.*, 1883, p. 19).

I have seen in painters a paralysis of one arm and one-sided wrist-drop, apparently the result of a local action of the poison; Dr. Manouvriez (*Recherches cliniques sur l'Intoxication saturnine locale et directe*, Paris, 1874) has recorded similar observations. (See also *La France Méd.*, 1882, i. 892.)

In those cases of lead-poisoning which pursue a slow course to death, the paralysis involves after a time the extensors of the lower as well as of the upper extremities, epileptic paroxysms occur at intervals, racking pains shoot through the limbs, points of cutaneous anæsthesia appear, and often albuminuria aids in producing the fatal issue. Gradually the patient becomes more and more cachectic, general œdema, with the whitened skin, betrays the increasing anæmia, the paralysis extends from muscle to muscle, locomotion becomes impossible, and, if a convulsion or other accident do not close the scene, death at last takes place from loss of power in the respiratory muscles. M. Malassez has found that in the anæmia of lead-poisoning the red globules are not only diminished in number but also increased in size (*Archives de Physiologie*, 1874, p. 50).

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* Consult *Deutsch. Med. Wochenschrift*, 1883, p. 185, 351; 1884, p. 129; also Dr. Paul Musehold, *Die Bleivergiftung, eine Ursache chronisch. Nierenerkrankung*, Berlin, 1883.

After death lead has been frequently found in the tissues. Heubel found most of it in the bones, and less in the muscular than in the nervous system (*Virchow and Hirsch's Jahrbücher*, 1871, vol. i. p. 316). Prof. Chatin (*Comptes-Rendus Soc. Biolog.*, T. iv., 1862, p. 84) obtained from the cervical spinal cord three in one hundred and fifty parts. In the studies of Ellenberger and V. Hofmeister (*Arch. Wissen. und Prakt. Thierheilk.*, x. 216) the liver and kidneys were found to contain the most lead, after them the bones, nerve-centres, and finally the flesh.

The electro-muscular contractility is affected very early in lead-poisoning, and may be lost before the voluntary movements. It is stated by M. Raymond that the short extensor of the thumb preserves its function when all the other extensor muscles are paralyzed. The paralyzed muscles are finally exceedingly wasted, and their structure may be so totally destroyed that scarcely a single striated fibre can be found. The nerve-trunks are lessened in size, in many of their tubules the medulla has been replaced by fatty granules, and in some cases every trace of the tubules has disappeared and the nerve been reduced to a fibrous cord. According to the researches of M. Dégérine (*Compt.-Rend. Soc. Biolog.*, 1880), the first appearance of change in a nerve-trunk consists in the myeline becoming broken up into blocks, and the nature of the change is a commingling of a parenchymatous and interstitial neuritis, which both Dégérine and M. Vulpian have traced upwards as far as the anterior spinal roots. Lancéraux (*Gaz. Méd. de Paris*, 1862, 1871), Westphal (*Arch. . Psych.*, Bd. iv. 776), Friedländer (*Virchow's Arch.*, lxxv. 24), and others may be cited as having found very distinct peripheral lesions in lead-poisoning. Whether these lesions begin in the nerve or in the muscles cannot be considered as determined. Birdsall (*N. Y. Med. Record*, March, 1882) reported a case of what he believed to be a plumbic myositis, and Gourbault (*Le Progrès Méd.*, 1880) describes primary alteration in the nerves, similar to those seen after section, as occurring in poisoned guinea-pigs, whilst MM. Debove and Reaut (*Le Progrès Méd.*, 1876, 151) describe the first changes as resembling those of subacute myositis, and Friedländer emphatically asserts that lessening in the size of the muscular fibres and multiplication of the muscular nuclei precede the nerve-degeneration. On the other hand, Vulpian (*Malad. du Système Nerv.*, 1879), Monakow (*Arch. f. Psychiat. und Nervenkr.*, Bd.

x. 495), and Oeller (*Festschrift dem Arztl. Verein München*, 1883) have observed structural changes (poliomyelitis, capillary hemorrhages, etc.) in the spinal cord of men dead of plumbism: whilst Popow (*Virchow's Archiv*, Bd. xciii. p. 351) found that when guinea-pigs were rapidly poisoned (six to eight days) with lead there was produced a central myelitis, which first affected the large cells of the gray matter, and afterwards involved the white matter, the peripheral nerve-filaments remaining normal.

There is, however, no real contradiction, as Popow believes, between his observations and those of Goubault, for the latter (*Arch. de Physiol. Norm. et Path.*, 1873) poisoned his animals very slowly (six months), and it is not improbable that the rapidity of the poisoning should have influence upon the seat of the lesion. As already stated, the symptoms of plumbism may exactly simulate those of general poliomyelitis, and Dégérine has found degeneration of the motor cells. The evidence at present indicates that lead is capable of producing a peripheral neuritis, and also a centric poliomyelitis; the probabilities being in favor of a peculiar peripheral neuritis, as the primary lesion of ordinary plumbic wrist-drop. Hemorrhages into the nerve-centres sometimes occur (*Progrès Méd.*, xii. 827).

Rudolf Maier (*Virchow's Archiv*, Bd. xc. 480) has found that the intestinal mucous membranes and walls suffer, in animals poisoned with lead, changes similar in nature to those already detailed as occurring in the kidney; and has also shown that there is widespread degeneration of the arterioles. It would appear that lead is an almost universal poison to the higher tissues, and that at present we are unable to say why in any individual case one part rather than another is attacked.

The excretion of lead with the gall is very active, but it is probable that it chiefly escapes from the body with the urine. The elimination seems to be capricious, and much affected by iodide of potassium (Melsens, *Ann. Phys. et Chem.*, xxvi.; Pouchet, *Arch. de Physiol.*, xii. p. 74) and by other influences.*

The treatment of chronic lead-poisoning evidently arranges itself under three indications: 1st, to prevent the ingestion of more of the poison; 2d, to aid in the elimination of that in the system; 3d, to relieve symptoms and restore lost functions. In lead-colic both of the last two indications are met by purgatives, to which opium should be added to relieve pain. It is often necessary to use the most powerful drastics, such as croton oil; but senna, salts, and other of the milder cathartics should always be tried first. *Alum*, it is asserted, acts in some unknown way as a specific in lead-colic, and from twenty to sixty grains of it may be given four or five times a day; but my own experience is not favorable to its use. In the more chronic forms of lead-poisoning, to fulfil the second indication baths of sulphuret of potassium should be employed, and iodide of potassium be administered internally. The bath should be given (Dr. A. Eulenburg, *Deutsches Archiv für Klin. Med.*, Bd. iii. p. 506) in a wooden tub, two or three times a week, and should contain six or seven ounces of the salt. The patient, during the half-hour of his continuance in it, should be from time to time well rubbed with a coarse towel. On coming out he is to be thoroughly washed with warm soap-suds. The dose of the iodide should be from fifteen to twenty grains, administered after meals, in dilute solution. A case is reported in the London *Lancet*, 1876, ii. 53, in which galvanic baths were used successfully, the patient being placed in the bath and the positive pole of a twenty-eight-cell battery applied to nape of neck, the negative to the feet. When severe cerebral symptoms arise, treatment is of little avail, and should be largely expectant.*

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* Lead has been found in the urine of man or animals by Orfila, Lewald (*Ausscheidung der Arzneimittel*, Breslau, 1861), Gusserow (*Virchow's Archiv*, Bd. xxi.), Annuschat (*Arch. Experim. Pathol. und Pharm.*, x. 260), and Oettinger (*Wiener Wochenschrift*, 1858); also in my clinical service at the University Hospital.

The local use of electricity is exceedingly important to restore the lost function of nerve and muscle. When the faradaic current elicits a response it should always be employed; but in some cases (*Meyer's Electricity*, New York, 1869, p. 284) the continued current retains its power after the induced has lost all its influence. The rule is always to apply that current which causes contraction; if both fail, the continued current should be used, the poles being reversed at intervals of four or five seconds. The electrical séances should be tri-weekly, each lasting about fifteen minutes, and they should be persevered in for months. I have seen great improvement in a case which for the first four months yielded no results; indeed, long after voluntary movement had in great measure returned, no form of electricity would cause contraction of the affected muscles.

PHYSIOLOGICAL ACTION.—The symptoms of acute lead-poisoning are chiefly due to its local irritant action, but those of chronic poisoning are of wider significance. How the lead is absorbed to produce them is uncertain, probably as an albuminate. All of the compounds of lead and albumen as yet discovered by the chemist are, however, precipitated by alkaline carbonates, and cannot therefore exist in the blood.

The symptoms of chronic lead-intoxication to be accounted for are the colic, the anæmia and wasting, the palsies, the rare cases of cerebral symptoms, or of kidney degeneration. In explaining them we are chiefly indebted to the researches of Dr. Ernest Harnack (*Archiv für Experim. Pathologie*, 1878), who employed the compound of lead and ethyl, first discovered by Loewig. When this is injected into animals in large quantities it causes a rapidly fatal train of symptoms, evidently due to the action of the compound itself. When, however, the introduction into the system has been slow, a chronic poisoning is produced by the lead set free in the blood and tissues.

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* It seems doubtful whether the sulphur baths really aid elimination, but I have certainly seen good follow their use. It has been denied that the iodide acts, but cases are reported in which lead was not in the urine before, and was after the administration of the drug (see *British Med. Journ.*, 1880, ii. 1034).

Under these circumstances a constant symptom, both in dogs and rabbits, is diarrhœa, due to a violently increased peristalsis, with, in the dog, occasional attacks of colic. As both the diarrhœa and the excessive peristalsis are arrested by atropia, they are probably the result of an action upon the intestinal ganglia. The colic in man is probably due to the excitement becoming so intense as to cause spasmodic contraction of the muscular coat of the intestine and consequent arrest of peristalsis, obliteration of the intestinal lumen, and constipation. If such be the case, large doses of belladonna should at once give relief.

Dr. Harnack found that in dogs the lead ethyl produces violent excitement, with chorea, convulsions, etc., evidently due to an exciting or irritant action upon the cerebrum, and believes that this explains the saturnine cerebral cases sometimes seen in man. Curci is stated to have proven that lead exerts an irritant influence upon the peripheral branches and ganglionic centres of the pneumogastric (*Gaz. Hebdom.*, 1883, 552; from *Gazze degli Ospitale*, Mars, 1883).

The chief symptom of the poisoning in frogs was a progressive palsy of muscular origin. The muscle became exhausted on repeated galvanization much more rapidly than is normal, and after death was incapable of undergoing complete post-mortem rigidity. The peripheral nerves appeared to have escaped entirely. The heart-muscle shared the fate of the voluntary muscles. The muscular action of the poison was excessively pronounced in rabbits, but was feeble in dogs and cats. Different results have, however, been arrived at by Dr. H. v. Wyss (*Virchow's Arch.*, Bd. xcii.), who found that the loss of reflex activity, etc., in the frog was not prevented by tying an artery so as to protect the leg from the poison; and that the protected muscle lost its power of responding to electrical stimulation just as fast as did the one reached by the lead. He concludes, therefore, that the paralysis is of centric origin.

The pulse in lead-colic is usually very hard and tense. Sphygmographic studies made of it by August Frank (*Deutsch. Arch. f. Klin. Med.*, xvi. 422, and Ernest Bardenhewer, *Berlin Klin. Wochen.*, 1877, 126), have been thought to indicate a condition of general arterial spasm, and have given rise to the very improbable theory that the colic is caused by intestinal anæmia from vaso-motor contraction. Bardenhewer found that hypodermic injections of pilocarpin relieve simultaneously the pulse and the colic precisely as Harnack discovered that atropia does. Harnack, however, found that in rabbits and dogs the lead ethyl has no action upon the circulation except by direct influence on the cardiac muscle, and that it does not produce vaso-motor spasm. He is probably correct in believing that the pulse of lead-colic is due to an overfulness of the blood-vessels, produced by an expulsion of the blood from the intestines by the severe spasm of their coats. According to the researches of Ellenberger and Hofmeister, in the sheep toxic doses of lead greatly depress the elimination of urea.

The following preparations of lead are officinal in the United States Pharmacopœia:

PLUMBI OXIDUM—OXIDE OF LEAD. U.S.

Litharge, which is prepared by blowing air through melted lead, occurs in small yellowish or orange-colored scales, which are insoluble in all ordinary menstrua. It is rarely used as a desiccant astringent powder for ulcers, but its chief employment in medicine is as the basis of the following preparations:

Emplastrum Plumbi, or *Lead Plaster*, is made by boiling litharge, olive oil, and water together. Glycerine is set free, and the oleo-margarate of lead is formed. Lead plaster occurs in grayish, cylindrical rolls, which become adhesive at the temperature of the body, and, spread upon kid, is sometimes used as a protective to parts exposed to pressure, or to superficial ulcers or abrasions. *Emplastrum Resinæ*, or *Resin Plaster*, or *adhesive or sticking plaster*, is made by incorporating resin with lead plaster, and, spread upon linen, is much used in surgery for mechanical purposes. The *Emplastrum Saponis*, or *Soap Plaster*, is made by the addition of soap to lead plaster. It is employed chiefly as a protective.

PLUMBI ACETAS—ACETATE OF LEAD. U.S.

Sugar of lead is made by the action of acetic acid upon litharge, or upon sheets of lead exposed to the air. It occurs in transparent, acicular, often aggregated crystals, of a sweet, styptic taste. It is soluble in water, to which it usually imparts a slight milkiness. From its solution it is precipitated black by sulphuretted hydrogen, white by soluble carbonates, chlorides, and sulphates, and bright yellow by the iodide of potassium. It is also incompatible with the mucilage of slippery elm, but scarcely so with that of flaxseed or of pith of sassafras.

THERAPEUTICS.—A solution of the acetate of lead is used very largely in acute external *inflammations* as a sedative and astringent lotion. Although chemically incompatible, it is frequently combined very advantageously in these cases with opium. As a too concentrated solution acts as an irritant, the strength for use on the skin should not exceed ten grains to the ounce. In diseases of the eye it is condemned by oculists, because when there is any abrasion of the cornea it is very prone to deposit an opaque film.

Internally, acetate of lead has been employed very largely in *hemorrhage*: indeed, Prof. George B. Wood commends it as the most valuable of all astringents in *hæmoptysis* (*Therapeutics*, vol. i. p. 158). I think it is now, however, rarely used for this purpose. Its chief use at present is in *diarrhœa*. On account of its sedative properties, when the purging is attended with inflammation it is the most serviceable of all the astringents; and, owing to the promptness of its action, it is also very valuable in cases with profuse serous discharges. In *dysentery* it is very useful whenever the discharges have become copious. The dose is from two to five grains, always in pill, repeated *pro re nata.* The *suppositories* (*Suppositoria Plumbi*, U. S. 1870) contain each three grains.

LIQUOR PLUMBI SUBACETATIS.—The *Solution of the Subacetate of Lead*, or *Goulard's Extract*, as it is sometimes called, is a colorless, limpid liquid, of a sweetish, astringent taste. It is made by boiling litharge in a solution of the acetate of lead, and has an alkaline reaction. When exposed to the air, it rapidly absorbs carbonic acid and deposits the carbonate of lead, the neutral acetate being left in solution. In its action upon the human organism, Goulard's extract resembles very closely the simple acetate of lead; but it is never used internally. Externally, it is a favorite application in cases of sprains or bruises, as well as in superficial inflammation. For this purpose it requires dilution, and from a fluidounce to four fluidounces of it may be added to a pint of water. When used upon a raw surface, the strength should not be so great. A sedative poultice, which is very highly recommended by some physicians in the early stages of inflammation, may be made by saturating crumbs of stale bread with Goulard's extract diluted with four to six times its bulk of water. This poultice must be applied cold. The officinal *Liquor Plumbi Subacetatis Dilutus*, or Dilute Solution of the Subacetate of Lead, is of the strength of three parts in a hundred. It is too weak to be of much value.

PLUMBI CARBONAS, U. S., or *Carbonate of Lead*, is a heavy, white, tasteless powder, insoluble in distilled water, but slightly so in water containing carbonic acid. It is used solely as an external sedative application. Rubbed up with linseed oil, it constitutes white-lead paint, and in this form, or in that of the ointment (*Unguentum Plumbi Carbonatis*, U. S.), it is a most efficient dressing for fresh burns. Care must be taken in its use, however, when a large surface is involved, as lead-colic has been caused by its absorption.

PLUMBI NITRAS, U. S., or *Nitrate of Lead*, occurs in white, nearly opaque, octahedral, very heavy crystals, soluble in alcohol and in seven and a half parts of cold water. It is used chiefly as a disinfectant. Dissolved in water, it forms *Ledoyen's Disinfectant Solution.* It acts by decomposing the sulphuretted hydrogen, itself being converted into a sulphuret of lead. It is said to attack actively the soldering of pipes (*Report on Hygiene*, U. S. Navy, 1879). Its chemical reactions are similar to those of the acetate, from which it may be distinguished by a mixture of it and sulphuric acid striking a red color with morphia. The nitrate of lead is frequently used in *onychia maligna.* The dead part of the nail should be cut away, and the powdered nitrate thickly sprinkled over the surface; after a few days the slough separates, leaving a clean surface, upon which the new nail usually soon forms. Sometimes more than one application of the remedy is required.

BISMUTHUM—BISMUTH.

The metal bismuth is never used in medicine in its simple or metallic form.

BISMUTHI SUBCARBONAS—SUBCARBONATE OF BISMUTH. U.S.

$(BiO_3CO_2,HO—2Bi_2O_3CO_3,H_2O.)$

A white or yellowish-white powder, tasteless and odorless, totally insoluble in water, soluble with effervescence in dilute nitric acid. The mode of its preparation is too complicated for discussion here, the chief object of the various steps being to get rid of the arsenic, which very generally contaminates the metal. The same assertions may be made in regard to the preparation of the Bismuthi Subnitras, or Subnitrate of Bismuth, U. S., a heavy white powder, odorless, with a faint acid taste, and a decidedly acid reaction when applied to moistened litmus-paper, insoluble in water, soluble without effervescence in nitric acid.

Physiological Action.—The actions of the subnitrate and of the subcarbonate of bismuth are so exactly similar that they can practically be considered as one thing; and for the sake of brevity I shall speak of these salts simply as bismuth, meaning thereby these preparations. Orfila and other of the old observers attributed to bismuth violent irritant properties, stating that severe symptoms, and even death, sometimes followed its ingestion; but these results were due not to the bismuth, but to the arsenic with which it was contaminated. When pure, however, it is free from any irritant properties, and is a feeble astringent and even a sedative, and can be taken without injury in indefinite quantity.

It has been denied that the subcarbonate and subnitrate of bismuth are dissolved in the alimentary canal, but we now know that they are very slowly absorbed and eliminated. Harnack affirms (*Arzneimittellehre*, 1883, p. 383) that the metal has been found by Orfila in the liver, spleen, and urine, and by Lewald in the milk. MM. Bergeret and Mayençon (*Journal de l'Anatomie*, 1873, p. 242) state that when the subnitrate of bismuth is administered the metal can always be detected, after a few hours, in the urine. They have also discovered it in the serous exudation of dropsy, and have proven that when a few grains of the salt mentioned are given to rabbits, in from twenty to thirty minutes it can be found in the urine, kidneys, spleen, blood, and muscles, and even eight days after the administration can be detected in all the tissues. Five days after the exhibition of a gramme of the subnitrate to a man, they found traces of the metal in the liver and kidneys; but the analysis of the body of a woman dead sixty-two days after the ingestion of two grammes yielded only negative results. Prof. E. S.

Wood also has detected bismuth in the urine four weeks after its last exhibition (*Tr. Amer. Neurolog. Assoc.*, 1883, p. 23).

THERAPEUTICS.—The preparations of bismuth are of great service in various forms of irritation of the alimentary canal. They are very useful to allay *vomiting* dependent upon gastric irritation. In simple neuralgic *gastric pain* following eating, especially when occurring in feeble, badly-nourished subjects, bismuth is often of great service; and even in *carcinoma* it may palliate by alleviating pain and vomiting. In *pyrosis* it is sometimes successful. In simple *diarrhœa* of irritation, and in the *chronic diarrhœa* of camps, the bismuth preparations are often very efficient; and in the chronic *bowel complaints* of children, especially as seen in the summer season, given with pepsin, they are almost invaluable. Topically, these preparations may be used with advantage as desiccant astringent applications in *leucorrhœa*, in *gonorrhœa*, and in *irritable external ulcers.*

ADMINISTRATION.—In order to be efficient, the bismuth preparations must be given in much larger doses than they were formerly used in. To infants five to ten grains may be administered at a dose, and to adults from twenty grains to a drachm.

BISMUTHI CITRAS. U. S.—The insoluble *citrate of bismuth* is not used in medicine, but has been introduced into the Pharmacopœia for the production of the *Bismuthi et Ammonii Citras*, U. S. The citrate of bismuth and ammonium is a soluble salt, which is much more astringent than the insoluble preparations of the metal, but at the same time more irritant. It lacks the peculiar virtues which grow out of the insolubility of the subnitrate, but has been used to some extent in doses of five grains in *chronic diarrhœa* and in *acute diarrhœas of relaxation.* It should be given in watery solution, repeated every three to six hours, according to the exigencies of the case.

CERII OXALAS. U. S.

The *oxalate of cerium* is a white powder, insoluble in water, alcohol, and ether, but soluble in sulphuric acid. It has been employed in medicine quite largely for the relief of *vomiting*, especially when dependent upon *pregnancy* or other forms of *uterine disturbance.* Its action on the economy has not yet been made out, but it may be tried with some hope of success in cases of nervous or dyspeptic vomiting. The dose is one to three grains, in pill, three or four times a day.

ZINCUM—ZINC.

ZINCI SULPHAS.—*Sulphate of Zinc.* U. S.—*White vitriol* occurs in irregular white masses, the *pure* sulphate of zinc in minute, transparent, four-sided, prismatic crystals, which effloresce slightly in dry air, and are soluble in two and a half times their weight of cold, and much less of hot, water; insoluble in alcohol. The taste is styptic and peculiar.

THERAPEUTICS.—The sulphate of zinc is in weak solution a stimulant astringent, in concentrated form an active irritant. Taken in doses of thirty grains it acts as a prompt, efficient mechanical emetic. In smaller doses, of two grains, it is sometimes given in pills as a stimulant astringent in *chronic diarrhœa* with ulceration.

TOXICOLOGY.—Sulphate of zinc in large doses acts as an irritant poison, producing violent vomiting, colicky pains, diarrhœa, prostration, etc. The symptoms which it causes are almost identical with those produced by the corresponding salt of copper. Alkalies and their carbonates are the chemical antidotes to it, producing insoluble precipitates. Eggs and milk should also be exhibited, and the symptoms treated as they arise. Chronic zinc-poisoning, if it really exists at all, is very rare, and the metal seems to be used with impunity in cooking utensils. Dr. Schlockow, however, affirms (*Deutsches Med. Wochensch.*, 1879, 208), that the zinc-smelters rarely live to be over forty-five; dying, sometimes with catarrh of the bronchial or alimentary mucous membranes, or, in other cases, of a peculiar nervous affection, which commences with burning superficial pains, exalted sensibility, and reflex activity in the legs, and afterwards puts on still more clearly the features of myelitis.

ZINCI OXIDUM VENALE.—*Commercial oxide of zinc* is a snow-white powder, obtained by burning the metal in the air. It should be used only in pharmacy. The *pure oxide* (ZINCI OXIDUM, U. S.) is made by heating the carbonate until the water and acid are driven off. It is a yellowish-white powder, insoluble in water, but soluble without effervescence in dilute acids.

THERAPEUTICS.—The oxide of zinc is used externally as a mildly astringent, slightly stimulant, and desiccant application in *skin diseases* and to *ulcers*. When given continuously in small doses it is believed to act as a tonic and alterative upon the nervous system. It has also been commended as an astringent in chronic *catarrhal diarrhœa* of adults and infants, and has been largely used in *epilepsy* and in *chorea*. The dose is two to fifteen grains. The *ointment* (*Unguentum Zinci Oxidi*, U. S.—one part to four of benzoinated lard) is especially useful in chronic *eczema*.

ZINCI CARBONAS PRÆCIPITATUS. U.S.—*Precipitated carbonate of zinc* is intended to replace the old impure native carbonate, *calamine*. It is made by precipitating the sulphate of zinc by the carbonate of sodium. It is a white powder, closely resembling in its properties the oxide of zinc.

ZINCI ACETAS. U. S.—*Acetate of zinc* is made by the action of acetic acid upon the commercial oxide of zinc. It occurs in white, micaceous crystals, which effloresce in a dry atmosphere and are very soluble in water. The taste is astringent and metallic. The acetate of zinc resembles in its physiological and therapeutic qualities the sulphate, but is probably somewhat less active. It is chiefly used in collyria (one to two grains to one fluidounce), and as an injection (five to twenty grains to one fluidounce) in *gonorrhœa.*

CADMIUM is employed in medicine to some slight extent in the form of its *sulphate*, which is stated to resemble closely the sulphate of zinc in its therapeutic properties. It has been especially used as an astringent stimulant in collyria, made by dissolving half a grain to four grains in an ounce of rose-water. Strangely enough, some physicians who have employed it state that it has ten times the strength of the zinc salt, others that it is about equivalent to it.

CUPRUM—COPPER.

CUPRI SULPHAS—SULPHATE OF COPPER. U.S.

The sulphate of copper occurs in blue, transparent, slightly efflorescent, rhomboidal prisms, or their fragments. It dissolves in four parts of cold and in two of boiling water, but is insoluble in alcohol. With ammonia its solution precipitates a bluish-white hydrated protoxide of copper, which redissolves when an excess of the alkali is added, forming a rich deep-blue solution.

PHYSIOLOGICAL ACTION.—In very dilute solution the sulphate of copper acts locally as a stimulant and mild astringent; in a more concentrated form it is an irritant; in powder it is a very mild caustic, which is scarcely capable of destroying sound tissue. Taken internally in very small amounts and continuously, it is thought to have a corroborant influence upon the nervous system. Prof. Falck (*Deutsches Klinik*, xi., 1859) has found that the sulphate of copper acts upon pigeons, dogs, rabbits, etc., as an irritant neurotic poison, producing great depression of temperature, with progressive general paresis ending in death, apparently from failure of respiration. When the copper salt was given hypodermically, vomiting was not produced; although when it was exhibited by the mouth, emesis was very violent and persistent. In doses of five to fifteen grains it acts upon man as an irritating emetic, and in larger amounts is an irritant poison.

THERAPEUTICS.—The chief internal use of sulphate of copper is as a mechanical emetic. As it is more irritating than sulphate of zinc, it acts more rapidly and in smaller dose. For the same reason, however, it is not so safe as the white vitriol, and cannot be repeated so freely when its action fails.

As a stimulant and astringent it is occasionally administered, in pill form, in *chronic diarrhœa* with ulceration. In small repeated doses it has been used in various nervous affections with doubtful advantage.

The chief value of the so-called "*blue stone*" is as an external application. When applied in solid form to ulcers, it destroys flabby granulations and exerts a powerful excitant influence. Its solution acts more feebly, and is sometimes employed as a dressing for indolent *ulcers*, but more frequently as a stimulant and alterant to mucous membranes, as in *granular conjunctivitis.*

TOXICOLOGY.—The symptoms of acute copper-poisoning generally come on in about a quarter of an hour after the ingestion of the poison, but may be postponed for from one to two hours. They consist of violent vomiting and purging, accompanied by very severe colicky pains. The matters vomited are greenish or bluish, the stools glairy, mucous, and at times bloody. There is a very strong taste of copper in the mouth, and often constant expectoration; excessive salivation and bronchial secretion are stated by Galippe (*Étude toxicol. sur la Cuivre*, Paris, 1875) to be characteristic. Death may occur in a few hours, preceded by convulsions, paralysis, delirium, anæsthesia, and other symptoms of great nervous disturbance, seemingly as the result of a direct action of the poison upon the nervous system. Sometimes a tendency to syncope is very marked. The urine is usually lessened or suppressed. Black urine, due to the presence of hæmoglobin without unaltered blood-corpuscles, has been noted; in this case, after death all the tissues were found stained with altered blood, and evidently destruction of the blood was an important factor in the fatal result (*N. Y. Med. Record*, xxi. 567); fatty degeneration of the liver was also found. If the patient survive for twenty-four hours, jaundice nearly always shows itself. After this, profound depression with nervous symptoms may develop and end in death; but not rarely a favorable issue results, in which case the symptoms of gastro-intestinal inflammation with fever develop themselves. In the experiments of Ellenberger and V. Hofmeister upon animals, hæmaturia and fatty degeneration of the liver were prominent phenomena (*Arch. Wissen. Prakt. Thierheilk.*, x. 228). The copper is said to be eliminated more freely with the salivary and intestinal secretions than with the urine (Galippe, *loc. cit.*, p. 41).

As the action of the sulphate of copper is exceedingly rapid, any antidote to be of avail must be given at once and act quickly. Milk and eggs are almost always at hand, and are the most efficient antidotes. No time should be lost in attempting to separate the yolk from the white of the egg, but the eggs should be broken into a bowl as quickly as possible, a little water added, and the whole stirred up and exhibited. The dose should be repeated several times, especially when there is vomiting. Soap or a fixed alkali may be given. The yellow *prussiate of potash*, when pure, is harmless, and precipitates instantly an insoluble compound of copper from solutions of its salt. When it is to be had in time, it may therefore be used as an antidote to the sulphate. The treatment of copper-poisoning after the administration of the antidote consists in meeting the indications as they arise; opium should be used freely. When death occurs, the results of gastro-intestinal inflammation are usually found; sometimes the intestine has a decided bluish tint, and occasionally submucous ecchymoses occur. In exceptional cases, it is said, there are no evidences of inflammation in the alimentary canal.* Fatty degeneration of the liver has been noted (*N. Y. Med. Rec.*, xxi. 567).

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* For a fatal case of repeated poisoning by copper, with much information of value to chemical experts, see *La France Médicale*, September, 1874, abstracted in *Half-Yearly*

If chronic copper-poisoning ever exist among workers in the metal, it must be very rarely. The chief symptoms are asserted to be "a coppery taste in the mouth, giddiness, pain in the bowels, vomiting, occasional diarrhœa, and wasting of the body." Dr. Clapton (*Medical Times and Gazette*, June, 1868) has pointed out, as characteristic, a *green* line upon the gums; this was also observed by Prof. Taylor, but its constancy is not assured. Thus, a green line was found on the teeth of all but two or three of a number of workers in the metal examined by a committee of the London Clinical Society (*Transactions*, 1870, p. 13), but there was no line on the gums of any of them. Galippe (*loc. cit.*) has brought forward much evidence to prove the non-existence of chronic copper-poisoning. Both he and Drs. Burcy and Ducom have found the metal almost without influence upon dogs (*Archives de Physiolog. Norm. et Path.*, 1877, t. iv. 183). Galippe (*Comptes-Rendus*, t. lxxxiv. 718) fed himself for one month on food containing a large amount of copper without causing any symptoms of intoxication. On the other hand, Dr. Faulk (*Deutsches Klinik*, ix. 376) asserts that the acetate of copper produces progressive paralysis, with failure of respiration and death.

CUPRI ACETAS. U.S.—*Acetate of copper* is in deep-green, prismatic crystals, yielding a bright-green powder; whilst the *impure subacetate*, or *verdigris*, occurs in masses of a pale-green color, which are often composed of minute silky crystals. Both acetates closely resemble the sulphate in physiological, therapeutical, and toxicological properties, but are less active.

ARGENTUM—SILVER.

ARGENTI NITRAS—NITRATE OF SILVER. U.S.

This is officinally prepared by heating together silver, nitric acid, and a small quantity of water. It is a heavy anhydrous salt, crystallizing in translucent, shining, rhombic plates, and having a styptic, exceedingly metallic, corrosive taste. It is soluble in its own weight of cold water. Muriatic acid or a soluble chloride throws down from its solution a white curdy precipitate *wholly* soluble in ammonia. For external use the crystals are melted and run into moulds, where they harden into round, grayish, brittle sticks, about the size of a goose-quill, and having a radiated crystalline fracture. These are the officinal *argenti nitras fusus*. As only the pure salt will make well-formed crystals, the impure products are always manufactured into the preparations just named, which should therefore not be employed internally. When the nitrate of silver, either in substance or solution, is exposed to the conjoint influence of light and of even a minute portion of organic matter, it turns

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Compendium, Jan. 1875. Bournevette and Yvon (*Revue Scientifique*, p. 859, 1874) found two hundred and ninety-five milligrammes of metallic copper in the liver of a woman who had taken the ammoniacal sulphate three months previously. Minute quantities of copper exist in the normal human body (*Bull. de Thérap.*, xciii. 88).

black, and is converted into an insoluble substance, which has been believed to be metallic silver, but is more probably an oxide. For this reason the white stains which it first makes when applied to living tissues soon blacken.

PHYSIOLOGICAL ACTION.—Nitrate of silver coagulates albumen, and, when applied in its pure state to living tissues, acts as a caustic, coating them over with a white almost membranous film. The caustic action is, however, not a deep one, because penetration of the salt into the tissues is soon prevented by the thick and tough skin or stratum which is formed. When applied in a dilute solution it acts as an astringent, constringing the vessels and overcoming relaxation. Its local action, however, is not simply that of an astringent, but is certainly peculiar and apparently alterative to nutrition.

When taken internally in sufficient dose, this salt, by virtue of its corrosive action, is a poison, producing gastro-enteritis; but it also acts directly upon the nervous system. Orfila and other of the earlier observers experimented upon it by injecting it directly into the veins of animals. When exhibited in this way, it must, by coagulating the albumen of the blood, produce thrombi, to which the subsequent symptoms are in greater or less measure to be ascribed. This method of experimentation can therefore throw but little light upon the action of nitrate of silver when taken into the stomach.

It is evident that in the stomach the nitrate of silver cannot long maintain its integrity. Dr. Bogolowsky has found (*Virchow's Archiv*, Bd. xlvi. p. 413) that when the nitrate is added to a peptone it is readily dissolved, and that the solution formed does not coagulate albumen.* That in this or in some other analogous form silver is absorbed is proven by its having been found in various internal organs and by the discoloration which follows its protracted use. When it is exhibited for a long continuous period, the skin often acquires a peculiar bluish slate color, which may become very dark, and in decided cases the conjunctiva and even the mucous membrane of the mouth are involved. The silver is found in all the tissues of the skin below the rete Malpighii † (Frommann, *Virchow's Archiv*, Bd. xvii. 135; Riemer, *Archiv d. Heilkunde*, Bd. xvi. 296; xvii. 330; Neumann, *Medizin. Jahrbücher*, 1877, 369). Prof. E. Harnack asserts (*Arzneimittellehre*, 1883, 410) that in all recorded cases of argyria at least thirty grammes of the salt have been taken. According to Dr. William Pepper, the staining of the skin is always preceded by a dark line upon the gums (*Trans. Philad. Coll. Physicians*, 1877). Both Heller and Orfila failed to detect silver in the urine of animals taking it; but probably it is eliminated, though slowly and in very small quantities, by the kidneys.

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* For recent studies of this character see Isedon Neumann (*loc. cit.*), also A. v. Fragstein (*Berlin Klin. Wochen.*, 1877, 294).

† In an elaborate study of the organs of a case of argyria, Riemer found the silver in the glomerules of the kidney, the intima of the aorta, the choroid plexus, and the mesenteric glands. He believes that it is never deposited inside the cells, but in the cellular tissue, and that the silver preparation is reduced in the intestines, and the fine particles of the silver carried in the blood and lymph. O. Loew (*Pflüger's Archiv*, xxxiv. 603) asserts, however, that the silver is deposited inside of the renal endothelium cells, and, as he has found that protoplasm has reducing powers, believes that the silver is reduced in the cells from a solution.

By an elaborate series of experiments, M. Chas. Rouget (*Archives de Physiologie*, July, 1873, p. 356) has shown that upon all animals from a crab to a dog the soluble salts of silver act as a poison, causing in mammals vomiting and purging, and in them and the lower animals violent disturbance of the motor functions, as shown by paralysis and convulsions, and of the respiration, ending finally in death by asphyxia. This is in accord with the observations of other investigators. MM. Rabuteau and Mourier have found that the almost instantaneous death which Charcot and Ball first noted as following the injection of a large dose of the nitrate of silver into the veins is due to a direct paralyzing influence of the drug upon the muscle of the heart. M. Rouget has never seen this form of death follow the hypodermic or internal administration of the poison, the heart always continuing to beat for a greater or less length of time after the cessation of respiration, and also retaining its irritability.

As already stated, both convulsions and paralysis are present in acute *argyria*, or silver-poisoning. The convulsions are severe, generally tetanic, and according to Rouget are plainly reflex. A peculiarity noted by Rouget is the persistence of the convulsions after the complete abolition of voluntary movements. M. Curci affirms that they are due to excitation of the motor tract of the cord, and that this is preceded by a similar influence upon the sensory tracts (*London Med. Record*, 1877, p. 72).

The death is due, in argyria, to cessation of the respiration; Rouget (*loc. cit.*, p. 351) even states that he has witnessed the suspension of the latter function in the frog whilst the activity of the reflex movements was much beyond normal. In the dog and in the full-grown cat this asphyxia is accompanied by an outpouring of mucus in the lungs, pulmonary congestion and œdema being found on post-mortem examination. Two theories have been propounded as to the cause of the asphyxia: one, that it is simply due to the choking up of the lungs by the congestion and the excessive secretion whose origin is an altered state of the blood; a second, that both the asphyxia and the lesions in the lungs have their origin in a direct action of the poison upon the nerve-centres.

The first view has been especially supported by Krahmer and by MM. Rabuteau and Mourier. Unfortunately, I have not seen the original papers of these physicians; but, according to Rouget, the basis of argument of Krahmer is simply the ecchymoses which he found in horses dead of the poison, whilst that of Rabuteau and Mourier is the fluidity of the blood after death, and the existence in it of globules which, on account of their solubility in ammonia, were believed to be the chloride of silver. The French observers were, however, almost certainly mistaken in their belief that these granules were chloride of silver, since ammonia dissolves hæmatin as freely as it does the chloride.

In 1864 Charcot and Ball (*Gazette Médicale*, 1864) made a series of experiments in which a silver salt that did not coagulate albumen was injected directly into the blood. They noted not only the respiratory embarrassment, but also that the hinder extremities were suddenly paralyzed, and concluded that both the asphyxia and the lung-trouble were due to an affection of the central nervous system. In 1869 Dr. Bogolowsky, of Moscow, studied (*Virchow's Archiv*, 1869, Bd. xlvi.) the action of a peptone of the nitrate when used hypodermically. He found, on examination of the blood of a poisoned animal, that the spectrum analysis (*loc. cit.*, p. 415) betrayed nothing abnormal; that the red corpuscles appeared paler and their outline more delicate than normal; that the white corpuscles were natural. On the other hand, Rouget (*loc. cit.*, p. 361) examined microscopically the blood of animals poisoned with the nitrate of silver, and found it perfectly normal. The only conclusion to be drawn from all this seems to me to be that at present there is no proof whatever that the symptoms of acute argyria are due to alterations in the blood. That the embarrassment of respiration is not due to local lesions in the lungs is abundantly shown by the experiments of Rouget, who found that whilst in all animals these respiratory symptoms are very prominent, in only a few species are decided pulmonic lesions found after death. From all these facts I think it highly probable, if not altogether certain, that the theory propounded by MM. Charcot and Ball is correct. That the motor disturbance is centric, not peripheral, in its origin, is shown by the fact noted by Rouget (*loc. cit.*, p. 354), that the muscles and nerves preserve their excitability after the arrest of the respiration.

The various facts which have been thus far brought forward in regard to the physiological action of silver, although interesting to the toxicologist, have very little reference to its therapeutic use, since it is never employed to produce an acute constitutional influence.

The action of the drug when exhibited continuously for a length of time in large doses has been investigated by Dr. Bogolowsky upon dogs and rabbits. He found that it produced loss of appetite, wasting, slight lowering of bodily temperature, diarrhœa, diminution of the quantity of urine passed, with increase of its specific gravity and often with the presence of albumen, and transitory paralysis. How far some of these symptoms were due to the direct constitutional action of the poison, and how far to derangement of the digestion dependent upon its local influence, is perhaps an open question. The local action was avoided, however, as much as possible, by the use of an albuminate or of the double phosphate of silver and sodium, which does not coagulate albumen. Comparative examinations of the blood showed that the hæmoglobin was reduced by more than one-third. The blood was also rendered very aplastic, as was betrayed by the constant tendency to the formation of ecchymoses. As some one has suggested that the silver in these cases replaces the iron of the blood-corpuscles, Dr. Bogolowsky made a chemical examination of the latter, but failed to find any traces of silver in them,—no doubt because it was not there. The solid tissues were found, after death from chronic argyria, to be in an advanced stage of degeneration, which especially affected epithelial structures. The first change was swelling and opacity of the cells, with obscuration of the nucleus. After this came fatty degeneration, fatty globules in the cell, destruction of nucleus, and finally of the cell itself. The liver and kidneys were profoundly influenced, as was also the muscular structure, especially of the heart. These results obtained by Bogolowsky have been in the main corroborated by A. V. Rózsahegzi (*Arch. Exper. Path. Pharm.*, ix. 295).

The summary which has been here offered comprises all our knowledge of the physiological action of the preparations of silver. Unfortunately, it does not throw much light upon their therapeutic use. The results of the chronic poisoning are so closely analogous to those produced under similar circumstances by antimony, arsenic, and probably other metallic poisons as to indicate that silver given internally acts upon the nutrition of the body,—in other words, that it is an *alterative*.

THERAPEUTICS.—By far the most frequent employment of nitrate of silver in therapeutics is for its local action, either upon the surface of the body or upon those mucous membranes that can be reached directly by the drug.

As a simple *caustic*, the salt may be used whenever only a superficial action is required; for reasons already given (page 45), it is useless whenever it is necessary to produce a deep eschar. As a *caustic* and an *alterative*, it is applied in solid form to many *ulcerated surfaces*, for the purpose of destroying superficial diseased tissue and of substituting, when the eschar separates, a healthy for an unhealthy action. As an *antiphlogistic*, nitrate of silver acts not only as an astringent, but also in some way not clearly understood. In the various inflammations of the mucous membranes, such as *conjunctivitis*, *faucitis*, *laryngitis*, *urethritis*, etc., it is employed very frequently, not only in the stage of relaxation, but in the beginning of the attack. In *conjunctivitis*, the solution employed should not, under ordinary circumstances, be stronger than one or two grains to the ounce; and it should not be used at all if any corneal ulceration exists, since a deposit of silver is liable to occur and to produce opacity. In *faucitis*, the strength of the solution may vary from thirty to sixty grains to the fluidounce. Even a saturated solution can scarcely be looked upon as caustic to the more robust mucous membranes. In ordinary cases of *sore throat*, the application once a day or every alternate day is generally sufficient. It is best made by means of a good-sized camel's-hair brush, each part of the inflamed surface being distinctly touched, and not the whole simply daubed or slopped over by means of a very large brush or a sponge probang, as is often done. In severe cases it may be necessary to use the solution twice a day. Dr. Carl Seiler affirms that whilst solutions of nitrate of silver of less than sixty grains to the ounce cause pain when applied to throat, solutions of one hundred and twenty to two hundred and fifty grains act as local anæsthetics, relieving soreness, and usually arresting acute inflammations at once, if applied in the first twenty-four hours before inflammatory exudation has occurred (*Jour. Amer. Med. Assoc.*, i. 266). In *laryngitis*, the solution may contain from ten to twenty grains to the ounce, and should be applied with a brush by the aid of the laryngoscopic mirror. An attack of *urethritis* may sometimes be aborted in its forming stage by the injection of a strong solution (grs. xii. to f℥i) of the salt; but the practice is of doubtful expediency, since when it fails it greatly aggravates the trouble. In the *advanced stages of gonorrhœa*, weak injections (grs. i or ii to f℥i) are often very serviceable.

Many years ago (1828) Mr. John Higginbottom originated the practice of treating *erysipelas* by the nitrate of silver, and his plan has received a great deal of commendation from authorities, but certainly has not been generally adopted by the profession. One or two cases of bad results, from ulceration of the skin apparently due to the local application, have deterred me from giving the method a fair trial, and I do not feel able to offer any opinion upon the practice. Mr. Higginbottom in a recent essay (*London Practitioner*, vol. ii. p. 34, 1869) reaffirms the value of the treatment, stating that its want of general adoption is due to its being so often imperfectly carried out, and gives the following directions:

> "The affected part should be well washed with soap and water, then with water alone to remove every particle of soap, then to be wiped dry with a soft towel. The concentrated solution of four scruples of the nitrate of silver to four drachms of distilled water is then to be applied two or three times on the inflamed surface, and beyond it on the healthy skin to the extent of two or three inches. The solution may be applied with a small piece of clean linen, attached to the end of a short stick, the linen to be renewed at every subsequent application. As the solution of the nitrate of silver is colorless, it is necessary to pass a little linen, just moistened, over every part where it has been used, in order to be equally diffused, so that no part may be left untouched. In about twelve hours it will be seen whether the solution has been well applied. If any inflamed part be unaffected, the solution must be immediately reapplied. Sometimes, even after the most decided application of the nitrate of silver, the inflammation may spread; but it is then generally much less severe, and is eventually checked by repeated applications. It is desirable to visit the patient every twelve hours until the inflammation is subdued."

In *superficial inflammations* other than erysipelatous I have frequently used nitrate of silver in this way, often with great advantage. Freely applied to the skin of the whole finger, it will sometimes even abort a commencing *felon*, or, applied to the scrotum, an *epididymitis*.

Internally, the nitrate of silver is exceedingly useful in stomachic and to a less extent in enteric diseases, exerting no doubt a purely local influence. In that form of *dyspepsia* characterized by the vomiting of large quantities of yeasty fluid, it has yielded in my hands better results than any other remedy; and the same may be said of *chronic gastritis* and of *gastric ulcer*. The rules of administration are identical in these three diseases. In the first place, regulation of the diet is imperative: if the case be a bad one, all eating of meals should be suspended, and the patient receive every two or three hours a cup of sweet milk, with sound toasted bread broken up and thoroughly softened in it. Nitrate of silver should be administered in pill form, one-quarter to one-half grain three or four times a day, taken when the stomach is empty. In very serious cases, when all food is rejected by the stomach, it is sometimes advisable to allow absolute rest for two or three days to that viscus, the patient being fed by the rectum, and only a little water and pills of silver with opium being taken by the mouth. Under these circumstances, the return to the usual method of taking food must be very gradual, at first only a tablespoonful each of milk and of lime-water being administered every hour. In *chronic enteritis* or *colitis*, nitrate of silver is sometimes of great service, especially if there be ulceration.

For its constitutional effects nitrate of silver is used solely in diseases of the nervous system. It was formerly given in *epilepsy;* but it has passed out of use. There is one serious objection to the employment of the salt,—namely, the discoloration of the skin which sometimes follows its continuous use. Again, it is not understood in what class of cases the drug is of especial value, and there is no means of judging as to its applicability to any individual case. When other means have failed, however, the nitrate of silver may be tried in epilepsy, the patient or his friends being informed that although with proper precautions the chances of discoloration are very few, yet it may occur.

In *chronic inflammations* of the spinal cord, whether affecting chiefly the posterior columns and constituting *locomotor ataxia*, or the anterior and giving rise to *paraplegia*, the nitrate of silver is one of the few remedies that are ever of any service; although it most frequently fails, yet it often does good, and in some cases has apparently even permanently arrested the disease. Dose, one-quarter to one-half a grain, always given in pill form: if it is desired to act on the stomach, the drug should be taken when the viscus is empty.

TOXICOLOGY.—The symptoms produced by the ingestion of large doses of nitrate of silver are partly gastro-intestinal and partly cerebro-spinal. In some cases the one series of phenomena predominate; in others, those of the other class. In a case at the Hôpital St.-Louis in 1839 (*Beck's Medical Jurisprudence*, vol. i. p. 675, Phila., 1863) the symptoms were insensibility, violent convulsions, and dilated pupils, with, on a partial return to consciousness, intense gastric pain; complete restoration of consciousness did not occur until eleven hours after admission into the hospital, and the coma returned at intervals during several days.

Vertigo, coma, convulsions, great muscular weakness, paralysis, with intense disturbance of respiration, are in these cases the manifestations of disturbed innervation; whilst the abdominal symptoms are those of gastro-enteritis. The diagnosis can generally be made by the discolorations of the lips and skin,—at first white, afterwards black,—and by the blackish or brownish vomit; when the customary antidote has been given, both vomit and stools are generally white and curdy. At post-mortem the stomach and bowels are found corroded, often ecchymosed and with patches of a white or grayish color. Poisoning by nitrate of silver is not common, and I know of but three fatal cases,—one in 1837 (Taylor, *Principles and Practice of Medical Jurisprudence*, second edition, vol. i. p. 319), one in 1861, a woman killed by fifty grains in solution in divided doses, one in 1871, a child destroyed by a piece of the solid stick three-quarters of an inch long, in spite of the immediate and free administration of the antidote (Scattergood, *British Medical Journal*, May, 1871).

The treatment consists in the administration at once of large amounts of *common salt*,—the chemical antidote,—the constant use of large draughts of milk, and the meeting of symptoms as they arise.

The fatal dose of silver varies very much, according, no doubt, as to the presence of substances capable of decomposing it in the stomach. Thirty grains have killed; and recovery has taken place after the ingestion of an ounce (case, Husemann, *Handbuch der Toxicologie*, Berlin, 1862, p. 868).

Chronic *argyria*, or discoloration of the skin by silver, is usually unaccompanied by disturbances of health, although in severe cases the discoloration affects not only the skin, lips, gums, sclerotic, but even the internal organs, such as the liver, spleen, kidneys. It is therefore not due, as has been thought, to the chloride of silver, since the latter only becomes dark under the influence of the light, but to a deposition of silver itself or of its oxide.* The minute quantity of the metal present is shown by the analysis of Versmanns (*Virchow's Archiv*, xvii., 1859), who in 14.1 grammes of dried liver found only 0.0068 gramme of metallic silver (0.047 per cent), and in 8.6 grammes of dried kidney 0.053 gramme (0.061 per cent.). Greater or less success has been claimed for various treatments in argyria, but in general they are equally futile. Rogers states that blistering will lighten the color very much, and Eichmann asserts (Husemann, *Toxicologie*, 871) that he has cured two cases by the use of potash baths and of soap baths, each four times a week. The older authorities commend the use of iodide of potassium internally. Dr. L. P. Yandell has reported (*American Practitioner*, June, 1872) two cases in which large doses of the iodide were given for many months for syphilis, and the mercurial vapor-baths used at the same time for the same purpose, with the result of a complete cure of the argyria. The fading was gradual.

ADMINISTRATION.—The nitrate of silver should always be given in pill, and, when it is desired to obtain its constitutional influence, after meals, during the process of digestion; but when its local action on the alimentary canal is required, it should be administered one or two hours before meals; and if the bowels are to be reached, the pill should have been made some time, so as to be dissolved as slowly as possible. When it is given in epilepsy or other chronic disease, its administration should be suspended for one week at the end of every third week, and its employment should not extend over a longer time than three months without a protracted intermission.

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* According to Rózsahegzi, Hermann has seen one case in which, preceding the deposition of the silver, there were malaise, emaciation, failure of memory, singing in the ears, deafness, and spasms of the ocular muscles.

Argenti nitras dilutus, U. S., is a grayish solid substance, often in crayons, composed of equal parts of the nitrates of silver and potassium. It may be used as a very mild caustic.

The *oxide of silver* (ARGENTI OXIDUM, U. S.) is an olive-brown powder, very slightly soluble in water, which the United States Pharmacopœia directs shall be prepared by precipitating the nitrate of silver with solution of potassa. It has been introduced into medicine as a substitute for the nitrate, with the idea that it would accomplish in diseases of the nervous system all that that drug is capable of, and at the same time not discolor the skin. With our present knowledge of the method of absorption of the nitrate, this seems highly improbable, and it is contradicted by experience. (Case, *Philad. Med. Times*, vi. 204.) Oxide of silver is not caustic when locally applied, but probably exerts some astringent action, and has been commended in *pyrosis*. In nervous affections it is probably of equal value with the nitrate. The dose is a grain, in pill, three or four times a day.

The *cyanide of silver* (ARGENTI CYANIDUM, U. S.) is used solely for the preparation of hydrocyanic acid. The *iodide* (ARGENTI IODIDUM, U. S.) has been used as an alterative, but is of very doubtful value.

CLASS II.—TONICS.

THERE are certain substances in nature which, when taken internally, act upon the nutrition of the various tissues so as to restore lost tone, not by calling into play the vital principle of contractility, but by increasing the power in the part. Such substances are known as tonics. They differ from astringents in that they affect nutrition, and consequently in the slowness and permanence of their action. They differ in a similar manner from simple stimulants, and as they do not call into sudden action forces already existent in the part, but increase power by increasing nutrition, their influence is a permanent one and is not followed by depression. They are, of course, indicated by debility dependent upon impaired nutrition,—*i.e.*, debility owing to actual loss of power. When the debility is due to a sudden depressing influence, as in snake-bite, they are of no service whatever. They are especially valuable in convalescence from acute disease; during the progress of the disorder they more often do harm than good.

Tonics should, of course, never be used when plethora exists. Sthenic inflammatory action is also a contra-indication to their employment; but when inflammation exists with a general state of debility, these drugs may form an essential part of the treatment.

The tonics are divisible into several sub-classes, which I shall consider separately.

SIMPLE BITTERS.

Probably all bitter vegetable substances possess tonic properties, but in many of them, as in morphia and strychnia, these properties are completely overshadowed by other inherent powers. There are, however, bitter vegetable substances which so act upon the stomach as to invigorate digestion, and to affect thereby the general nutrition, without exerting any direct influence upon other portions of the body than the alimentary canal. These are the simple bitters. In overdoses they nauseate, and may act slightly on the bowels. They appear all to act alike,—differing more in strength than in quality,—so that one may be substituted without detriment for another. As they are essentially irritants, inflammation or over-sensitiveness of the alimentary mucous membrane distinctly contra-indicates their administration. They are indicated by loss of appetite and loss of stomachic tone.

QUASSIA. U.S.

The wood of Simaruba excelsa, a large tree, native of Jamaica. This wood is light both in density and color, somewhat resembling that of the tulip-tree, but distinguished by its intensely bitter taste. It is kept in the shops in billets and in raspings. The active principle of it appears to be *Quassin*, an intensely bitter, neutral, crystalline principle discovered by Winckler (*Repert. für Pharmacie*, Bd. liv. 85, Bd. lv. 85). *Simaruba* (U. S.), the bark of Simaruba officinalis, also contains quassin, and may be substituted for quassia.

PHYSIOLOGICAL ACTION.—*Quassin* is said in large doses to be actively poisonous to insects, and even to mammals (Stillé's *Therapeutics*, i. 472; Husemann, *Die Pflanzenstoffe*, p. 718); but I have met with no detailed study of its action except that of I. Hoppe, who experimented upon frogs (*Deutsches Klinik*, xi., 1859). In doses of one grain it usually produced death in a short time. The symptoms were great weakness, with, in most cases, convulsions and sometimes convulsive tremblings, failure of respiration, and finally cessation of cardiac action. The functional activity of the nerve-trunks was much impaired, that of the muscles to a less extent. Locally, quassin appeared to act as an irritant as well as a powerful poison to both nervous and muscular tissues. Dr. Campardon found that in doses of five milligrammes of the pure crystalline form, or five centigrammes of the commercial amorphous variety, quassine acts upon a man as a powerful bitter tonic, notably increasing the secretion of bile and of the urine, and causing some looseness of the bowels and stimulation of the bladder. Fifteen milligrammes of the crystalline quassine caused violent frontal headache, burning pains in the œsophagus and throat, nausea, vomiting, vertigo, excessive nervous restlessness, diarrhœa, very frequent micturition, but diminished renal secretion (*Bull. Gén. de Thérap.*, ciii. 410).

THERAPEUTICS.—Quassia is probably the most active of all the simple bitters, and may be used whenever such remedies are indicated. In cases of *seat-worms* in children, a strong infusion of quassia (℥ii to Oj) affords a most harmless and efficient injection. Its exhibition should be preceded by an enema of simple water, after a stool, so as thoroughly to wash out the rectum and allow access to every fold of the rectal mucous membrane. The officinal preparations are a *tincture* (*Tinctura Quassiæ*—1 to 9, U. S.), dose, twenty drops to a teaspoonful; a very excellent watery *extract* (*Extractum Quassiæ*, U. S.), which may be given in pills containing from one to three grains; and a *fluid extract* (*Extractum Quassiæ Fluidum*), dose, five to ten drops.

GENTIANA—GENTIAN. U. S.

The root of the Gentiana lutea, or yellow gentian of the Alps. This root occurs in the shops either in pieces of various size and shape but generally several inches in length, or else in transverse slices. The texture is spongy, the odor faint but peculiar, and the taste bitter. It contains *gentisic acid*, which was discovered by Leconte, and is tasteless and physiologically inert. The active principle is probably the *gentiopikrin* of Kromayer, a neutral, crystalline substance, of an intensely bitter taste.

THERAPEUTICS.—Gentian is one of the most efficient of the simple bitters, and may be used whenever such a remedy is indicated. It is never given in substance, but in one of its preparations. These are the *compound tincture* (*Tinctura Gentianæ Composita*, U. S.), which contains gentian (1 to 12.5), bitter-orange peel, and cardamom—dose, one fluidrachm to half a fluidounce; the watery extract (*Extractum Gentianæ*, U. S.), dose, two to four grains, and the *fluid extract* (*Extractum Gentianæ Fluidum*, U. S.), dose, ten minims to half a fluidrachm. The *compound infusion*, formerly officinal, was a valuable preparation, containing some alcohol, and much used in doses of one to two fluidounces.

NECTANDRA.

Bebeeru Bark is the bark of the Nectandra Rodiei, a large tree which grows in Guiana and the neighboring parts of South America and is used in ship-building under the name of Greenheart. It occurs in large flat pieces, and contains an alkaloid, which was discovered by Dr. Maclagan, of Edinburgh. According to the researches of Walz (*N. Jahrb. Pharm.*, xii., 1861, 302) and of Flückiger (*Ibid.*, 1869), this alkaloid is identical not only with *Buxia*, obtained by Fauné in 1830 from Buxus sempervirens, but also with *Pelosia*, discovered by Wiggers in pareira brava. *Bebeeria*, or, as it should be called, *buxia*, is whitish, amorphous, inodorous, very bitter, very slightly soluble in water, freely so in ether and alcohol, and forms uncrystallizable salts. Dr. Maclagan found a second alkaloid, *Sipeeria*, in bebeeru bark, but it is probably only altered bebeeria.

PHYSIOLOGICAL ACTION.—Our knowledge of the influence of bebeeria upon the system is exceedingly incomplete. Albers (*Virchow's Archiv*, Bd. xxiv.) found that three grains introduced beneath the skin of a large frog produced death in six and a half hours. There was first a period of quiet with accelerated breathing, then tonic and clonic general convulsions, seemingly associated with muscular weakness, but with no increase of the reflex activity. Prof. Binz (*Virchow's Archiv*, Bd. xlvi. p. 130) has determined that bebeeria exerts some destructive influence over infusorial forms of life, but that it is in this respect not nearly so powerful as the cinchona alkaloids.

THERAPEUTICS.—Bebeeria was originally proposed by Dr. Maclagan as a substitute for quinia in malarial diseases, and has been quite extensively tried. It appears to possess some antiperiodic powers; but they very probably are not superior to those of the more powerful simple bitters, and are certainly very inferior to those of quinia, so that bebeeria is at present very seldom if ever used. The sulphate, which is officinal in the British but not in the United States Pharmacopœia, may be given in acidulated solution in doses of from two to five grains.

BERBERIS—BARBERRY.

Under the above title the U. S. Pharmacopœia of 1870 recognized the bark of the root of Berberis vulgaris, a native of Europe. This drug contains the alkaloid berberina, which, although not itself officinal, is found in so many recognized drugs as to require notice.

Berberina occurs as a yellow powder, or in fine yellow needles or prisms, of a bitter taste and neutral reaction, moderately soluble in cold, freely in hot, water, freely soluble in alcohol. With acids it forms mostly crystallizable, golden-yellow salts.

Its effects upon animals have been studied by Falck and by Guenste. In dogs it produced, when given in very large doses, restlessness, convulsive tremblings, thirst, and diarrhœa, and finally partial paralysis of the hind legs. From seven to fifteen grains of it killed rabbits in from eight to forty hours. The symptoms were increased frequency of respiration, and tremblings, followed by decrease of the rate of breathing, paresis, paralysis of the hind legs, great dyspnœa, and finally convulsions. In man, as yet, no serious symptoms have been recorded as produced by berberina. Buchner took nearly twenty grains without causing anything more serious than a loose stool. As a bitter tonic it has been used by various physicians in doses of from two to five grains, and its action in this dose appears to be that of a simple bitter. It may be given in pill form or dissolved in alcohol.

CALUMBA—COLUMBO. U.S.

The root of Cocculus palmatus, a climbing vine of Mozambique. It occurs in the shops in transverse disk-like slices, oval or circular in outline, one or two inches in diameter, of a spongy texture, having a yellowish surface, very bitter taste, and slightly aromatic odor. It contains a great deal of starch, besides berberina, and, it is said, in lesser amount, *Columbin*, a bitter neutral principle crystallizing in rhomboid prisms or needles.

THERAPEUTICS.—A bitter, slightly aromatic tonic, useful as a stomachic in cases in which a simple bitter is indicated. It is not used in substance. Its preparations are—a *tincture* (*Tinctura Calumbæ*—1 to 9, U. S.), dose, one to two fluidrachms; and a *fluid extract* (*Extractum Calumbæ Fluidum*, U. S.), dose, fifteen minims to half a fluidrachm.

EUPATORIUM—BONESET. U.S.

The herbal parts, gathered after flowering, of the indigenous Eupatorium perfoliatum, a tall, coarse composite, recognizable by its perfoliate leaves, through whose centre grow the stems and branches. This drug given in cold infusion (℥i to Oj—dose, f℥i–ii) is an efficient but disagreeable bitter tonic. Its chief employment is as a sudorific. The hot infusion when taken freely (five to six ounces), the patient being well covered in bed, produces free sweating, and has been very largely used in "general colds," *muscular rheu-*

matism, etc., for this purpose. The only objection to the remedy is its disagreeable taste. In the dose of a pint the infusion has been employed as an emetic. The *fluid extract* (*Extractum Eupatorii Fluidum*, U. S.) may be used in doses of a fluidrachm to a fluidounce.

CHIRETTA, U. S., the herb and root of a plant growing in the northern part of India, is one of the best of the simple bitters, and is believed by some to exert a peculiar influence over the liver. Whenever a simple bitter is indicated, this drug may be employed, especially if a cholagogue action be desired. The *solid extract* is an excellent preparation in doses of one to two grains; the *fluid extract* (*Extractum Chirettæ Fluidum*, U. S.) may be given in doses of five to ten minims; and the *tincture* (*Tinctura Chirettæ* —1 to 9, U. S.) in doses of a fluidrachm.

CORNUS. U. S.—*Dogwood*, the bark of the Cornus Florida, is feebly tonic, and has been supposed to be antiperiodic. It is very rarely, if ever, used by regular practitioners of medicine, and may be given in almost indefinite doses.

PECULIAR BITTERS.

These are bitter vegetable tonics possessing other properties besides those of the simple bitter.

PRUNUS VIRGINIANA—WILD CHERRY BARK. U. S.

Wild cherry bark is the product of the Prunus (Cerasus) serotina or wild cherry tree, not of Prunus Virginiana or Choke cherry, whose name it bears. It occurs in pieces of various sizes, usually without epidermis. The color is a reddish cinnamon; the taste slightly astringent, bitter, and peculiar, resembling that of peach-leaves. It contains tannic acid, bitter extractive, amygdalin, and emulsin. *Amygdalin* is a nitrogenous, crystallizable, odorless glucoside, of a slightly bitter taste. It is soluble in water and alcohol, but not in ether. *Emulsin* is an albuminous principle, which is soluble in water, and, like other forms of albumen, is coagulated by heat, alcohol, acids, etc. When amygdalin in watery solution is brought in contact with emulsin, it is decomposed, forming prussic and formic acids and a colorless, thin, volatile oil, which, when pure, has a peculiar agreeable odor and a burning taste. According to Liebig and Wöhler (*Ann. Chem. Pharm.*, xxii. 1), seventeen grains of amygdalin yield one of hydrocyanic acid: therefore, if thirty-four grains of amygdalin be mixed with sixty-six grains of emulsion of sweet almonds, a two per cent. solution of hydrocyanic acid will be formed.

PHYSIOLOGICAL ACTION.—Amygdalin administered by itself is nearly, if not quite, without effect upon the organism. Widtmann and Denk (Husemann, *Die Pflanzenstoffe*, p. 688) took as much as sixty grains of it without inducing any effect, and their results have been confirmed by Reil and others.

Lehmann, it is true (*Ibid.*), found that at times fifteen grains of it by the mouth were sufficient to cause death in the rabbit, but Kölliker and Müller have shown that this was owing to its being converted into prussic acid by the emulsin contained in the green herbage in the stomach of the rabbit.

THERAPEUTICS.—In wild cherry bark properly administered there are three active ingredients,—tannic acid, bitter extractive, and prussic acid; and to their combined action the general effect is due. As the tannic acid is in small quantity, its influence is not marked; but probably some of the reputation which the remedy formerly enjoyed as being useful in the night-sweats of phthisis was due to it. When given in the ordinary dose, I have never been able to detect any sedative effect from wild cherry bark; but the infusion administered with sufficient freedom certainly ought to exert such influence. Prunus Virginiana is therefore slightly astringent, sedative, and, owing to its bitter extractive, tonic. It is frequently useful in *phthisis* when a roborant is needed and at the same time a calmative action on the nervous system is called for. It may be used in *hectic fever* from any source.

The *infusion* (*Infusum Pruni Virginianæ*—1 to 25, U. S.) is useful as an adjuvant to other tonics, especially sulphuric acid, in *debility* with a tendency to night-sweats during convalescence from acute disease. The dose is one to two wineglassfuls. On account of its pleasant taste and traditional reputation, the *syrup* (*Syrupus Pruni Virginianæ*, U.S.) is often employed as the basis of cough-mixtures. The *fluid extract* (*Extractum Pruni Virginianæ Fluidum*, U.S.) may be given in doses of from half a fluidrachm to a drachm.

CINCHONA. U.S.

Under the general term of Cinchona the United States Pharmacopœia recognizes the "bark of all the species of the genus Cinchona containing at least two per cent. of the alkaloids which yield crystallizable salts." Under the name of CINCHONA FLAVA, or YELLOW CINCHONA (syn. *Calisaya Bark*), the same standard list includes the bark of Cinchona Calisaya; under the name of CINCHONA PALLIDA, PALE CINCHONA, that of Cinchona Condaminea and C. micrantha; under the title of CINCHONA RUBRA, RED CINCHONA, that of C. succirubra.

All the trees yielding quinia and its congeneric alkaloids belong to the genus Cinchona, and inhabit the slopes of the Andes Mountains from the northern extremity of South America to the lower portion of the republic of Bolivia, at an altitude of from five to ten thousand feet. The bark is collected by persons known as *Cascarilleros*, and is exported in large bundles or bales, usually surrounded with raw ox-hide. To these packages the term *seroons* is applied.

The *Pale Bark* occurs in quills or cylindrical rolled pieces, with a grayish or brownish adherent epidermis. It derives its name from the light fawn-color of its powder.

The *Calisaya* or *Royal Yellow Bark* comes both in quills and flat pieces. The epidermis is absent, or, if present, is loosely attached. The powder is of a decidedly yellow color, sometimes almost orange. The fracture is short and fibrous, presenting semi-transparent, sharp spiculæ, which are apt to become detached and penetrate the fingers.

The *Cinchona rubra*, or *Red Cinchona*, occurs in quills and flat pieces. The epidermis is generally present, and is often very warty. The color of the powder is a faint reddish-brown. Beneath the epidermis is in most specimens a distinct, red, resinous layer, which is very apparent in cross-section.

Large quantities of bark under the name of *Carthagena Bark* find their way into commerce through the northern ports of South America. For descriptions of these the reader is referred to works on Materia Medica.

Very successful attempts are being made to cultivate cinchona, especially in the Himalaya Mountains, Java, and Jamaica, where many millions of the trees have been planted and are thriving. The East India bark is already arriving in London in considerable quantities, and in a few years the supply from this source will doubtless be very large.

CHEMICAL CONSTITUTION.—Besides tannic, kinic, and kinovic acids, and other important substances, the cinchona barks contain quinia and quinidia, cinchonia and cinchonidia. Out of these alkaloids quinicia and cinchonicia are readily formed artificially, but, so far as is known, they do not exist in nature. There are therefore two isomeric alkaloidal groups; quinia, quinidia, quinicia; cinchonia, cinchonidia, cinchonicia.

QUININA. U.S.

This alkaloid was first distinctly separated from the other ingredients of the bark by Pelletier and Caventou in 1820. When quinia is precipitated by an alkali from a solution of its salt, it usually falls as a hydrate, which may be crystalline. By sufficient heat the hydrate is melted and the water is driven off. On cooling, the alkaloid, now free from water, forms a white, opaque, crystalline mass.

The neutral, officinal *sulphate of quinine* (*Quininæ Sulphas*, U. S.) occurs in light silky crystals, soluble in seven hundred and forty parts of cold or in thirty of boiling water, readily soluble in alcohol, very freely so in acidulated solutions, nearly insoluble in ether. The aqueous solution, upon the addition of chlorine, and afterwards of ammonia, assumes a green color. According to Dr. G. Kerner, if the original solution be colorless and clear and in a clean test-tube, one-thirty-thousandth part of the alkaloid can be recognized by this chlorine-ammonia test. When to one hundred parts of the salt, dissolved in nineteen hundred and twenty parts of cold dilute acetic acid (sp. gr. 1.042), are added successively four hundred and eighty parts of alcohol (sp. gr. 0.837) and sixty parts of a saturated alcoholic solution of iodine, crystals of *Herapathite* separate, in the form of right-angled quadrate rhombic leaves, which when seen by transmitted light are olive-green, but in reflected light are bright metallic green, resembling the elytra of Spanish flies. When heated, the sulphate of quinia becomes phosphorescent, emitting a pale-green light at 155° to 160° C., and at a higher temperature melts with the development of purplish vapors. When the neutral sulphate of quinia is dissolved in water acidulated with sulphuric acid, it is converted into the soluble bisulphate, which may be obtained in orthorhombic prisms by evaporation.

PHYSIOLOGICAL ACTION.—Quinine or its salts in powder or solution are, when applied upon a part denuded of its epidermis, very active irritants. Upon the skin they have little or no influence, but upon the mucous membranes they exert a very perceptible stimulant or irritant action.

A. Eulenburg found that when quinia was brought into contact with a nerve it did not cause contraction in the tributary muscles, but when placed upon the muscles themselves it induced immediate violent action. He therefore concludes that it is not a nerve-irritant, but is a muscle-irritant. When it is administered to dogs in sufficient quantity, it produces restlessness, followed by muscular tremblings, which have been compared to those of paralysis agitans, loss of power deepening into more or less complete paralysis, great dyspnœa, and cerebral symptoms, such as anæsthesia, blindness, stupor, or violent delirium, dilated pupils, coma, and convulsions. When the drug is introduced by the stomach, vomiting generally occurs, and at times diarrhœa also.* Death has been shown by Heubach to be produced, at least in the lower animals, by a failure of the respiration.†

The first symptoms of cinchonism, as produced by small therapeutic doses (ten grains) in man, are usually ringing in the ears, slight fulness in the head, and perhaps some deafness. With the use of larger doses these symptoms are intensified: the deafness is very marked, disturbed vision‡ may exist, and the flushed face, with the sense of distention in the head, may point towards a cerebral congestion, which is in some cases relieved by spontaneous epistaxis. In decided cinchonism, giddiness and staggering in walking are very common. After toxic doses, severe headache, delirium, stupor, complete deafness and blindness, dilated pupils, embarrassment of respiration, great weakness, convulsions, paralysis, and finally collapse, may result, either comatose or delirious. The deafness produced by large doses of quinine usually passes off rapidly; very rarely is there a permanent impairment of hearing. Amaurosis, with a peculiar ischæmia of the retinal vessels, has in a small number of cases been produced by very large therapeutic doses of the alkaloid (see *Archives of Ophthalmology*, x. 81, 214, 220).

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* See M. F. Melier, *Mémoires de l'Académie*, t. xii. p. 722, 1843; Wm. O. Baldwin, *American Journal of the Medical Sciences*, April, 1847; P. Briquet, *Traité thérapeutique de Quinquina*, Paris, 1855.

† The present is perhaps as suitable a position as any to notice certain researches upon the relations of alkaloids to protoplasm. The relation between medicinal substances and the tissues upon which they act is certainly a very close one, and very probably is chemical in its nature. Dr. Rossbach (*Pharm. Untersuch.*, Bd. i., Hft. iii.) found that various alkaloids sensibly modify the properties of albumen, and believes that they form a chemical compound with it. Under the influence of the poison the albumen coagulates at a much lower temperature, and is deprived of its affinity for ozone. The alkaloids also precipitate the albumen from its ozonized solution.

‡ I have seen complete temporary amaurosis produced in a lady by twelve grains of quinine.

The minimum fatal dose of quinine is not known, but it must be large, and probably varies very much. Dr. Clapton details (*Medical Times and Gazette*, April, 1864) a case in which a soldier took at one dose an ounce of the sulphate, stirred up in some water, without the induction of any more serious symptoms than a mild stupor; a similar case is mentioned by Dr. Lente, on the authority of Dr. Woodhull; and a third is recorded by Taussig (Stillé's *Therapeutics*, vol. i. p. 507). Dr. R. G. Wharton records (*Amer. Journ. Med. Sci.*, April, 1844) a case in which during thirty-six hours a half-ounce was taken without vomiting and without ill effect. I cannot help suspecting that in all of these cases much of the drug passed through the intestines without absorption. In the famous case of Bazire five ounces taken in the course of ten days caused death. Von Graefe asserts that he has seen two cases of amaurosis caused by quinine; the sufferer in one instance taking half-drachm doses until six drachms were ingested, in the other case an ounce altogether of the drug.

A close physiological study of quinia can best be made by investigating its effects upon the different systems of organs *seriatim;* and this shall now be done.

Cerebrum.—According to the experiments of Briquet, a solution of sulphate of quinia injected into the carotid will in some cases produce meningitis. In doing this, it is evident, the salt acts rather as an irritant to the membranes of the brain than as a nervous stimulant: indeed, experimental evidence proving that quinia is a cerebral stimulant seems to me to be wanting. The chief proof that the alkaloid does act as a stimulant lies in the fact that persons who have been taking it regularly for some time will occasionally, upon the sudden withdrawal of their daily dose, manifestly be less active without than with it. Briquet may be right in his belief that in small doses it acts as a nervous stimulant, but the proof of his correctness at present is clinical rather than experimental. When given in toxic doses to the lower animals, probably all of the cinchona alkaloids produce epileptiform attacks. Dr. J. Jakoubowich (*Revue des Sciences Méd.*, 1873) has noticed such effect with quinine in dogs, and it has been produced with cinchonidine in various animals. Chirone and Curci found that in the pigeon this action of cinchonidine is prevented by ablation of the cerebral hemispheres, but Prof. Albertoni objects with much force that these observers gave the pigeon the alkaloid too soon after the ablation, whilst it was still profoundly affected by the shock and hemorrhage of the operation (*Arch. f. Exper. Pathol. und*

Therap., xv. 278). Prof. Albertoni found that, if the pigeon was allowed to recover, the cinchonidine was capable of causing convulsions; also, that in dogs with the motor zone of the cerebral cortex destroyed, the alkaloid caused epileptiform attacks, and that therapeutic doses do not increase the excitability of the cerebral cortex in the dog. The subject is one of great interest in connection with the circumstance, noted for quinine by Brown-Séquard and confirmed by Albertoni as regards cinchonidine, that in epileptics the attacks are rendered decidedly more frequent by the cinchona alkaloids. The present evidence indicates that this increase is not due to an influence upon the cerebral cortex, but can hardly be considered sufficient to be conclusive. In very large doses quinia without doubt abolishes the functions of the cerebrum. Louis Dupuis (*L'Action physiol. de Quinine*, Paris, 1877) found that reflex action was normal in poisoned dogs and rabbits, although there was complete loss of sensibility, and he naturally concludes that the latter was of cerebral origin. The disorders of special sense produced by quinine seem to be the result of a direct or indirect congestive action upon the peripheral sense organs; since Dr. Kirchner (*Sitzungsberichte Phys.-Med. Gesells. Würzburg*, 1881, 161) found, in rabbits, cats, and guinea-pigs which had been poisoned with quinine or with salicylic acid, very great congestion of the internal ear and of the labyrinth, with bloody exudation, and with, in some cases, the ear-drum swollen into a bladder-like body by serous exudation. These observations of Kirchner are very interesting, as throwing light upon the cause of the *tinnitus aurium* and deafness of cinchonism; they are in close accord with the observations of Dr. Roosa (*Amer. Journ. Med. Sci.*, 1874), that sufficient doses of the alkaloid cause congestion of the blood-vessels connected with the human manubrium, *i.e.*, with the middle ear.

Spinal Nerves and Centres.—Schlockow was the first to notice a stage of increased reflex activity produced in the frog by quinia: its existence was subsequently denied by A. Eulenburg (*Reichert's Archiv*, 1865), but has been reaffirmed by H. Heubach (*Centralb. Med. Wissensch.*, 1874, 674), and by my pupil, David Cerna, who agree in finding that it occurs only after very minute doses. In his investigations made in the Laboratory of the University of Pennsylvania, Dr. Cerna found that this stage of excitement is probably caused by a stimulant influence upon the peripheral sensory nerves, as it did not occur when the abdominal aorta was tied previous to the exhibition of the alkaloid (*Phila. Med. Times*, x. 493). Two facts, first pointed out by Dr. T. A. Chaperon (*Pflüger's Archiv*, 1869, 295), have been so abundantly substantiated that we must accept them as established. They are—in *small* doses quinine causes in the frog a lessening of the reflex activity, which is removed by section of the medulla, but in *large* doses it produces a permanent palsy of reflex activity. The first of these actions has usually been considered to show that the alkaloid stimulates Setschenow's centre in the base of the brain, but Dr. Sedgwick (*Jour. of Physi-*

ology, iii. 22) believes that the inhibition is such as occurs when a sensitive nerve is galvanized, and is the result of a stimulation of the peripheral afferent cardiac pneumogastric nerve endings. He bases his theory chiefly on the fact which he has discovered that atropia prevents the primary inhibition of reflexes by quinia. This is, however, readily explainable without the adoption of the theory of Sedgwick, and as the results which he obtained after division of the pneumogastrics are scarcely in accord with his theory, it is still most probable that quinia is a stimulant of Setschenow's centre. The cause of the permanent influence upon reflex activity has not yet been accurately determined. Chaperon has shown that the motor nerves are unaffected, but this does not prove that the spinal centres are paralyzed. A. Eulenburg (*Reichert's Archiv*, 1865) asserts that voluntary movements persist after reflex actions, and that the quinized frog will turn into its normal position when laid upon its back, although ordinary reflex actions are completely abolished. This, if correct, certainly shows that it is either the sensory nerves or the receptive centres of the cord whose paralysis by quinine puts an end to ordinary reflex movements. So that, accepting the various results reached by experimenters, it is probable that in frogs quinine first excites and then paralyzes the peripheral sensitive nervous system. How far this applies to man is uncertain. According to the experiments of H. Kobert (*Archiv f. Exper. Pathol. und Therap.*, xv. 49), very large doses of cinchonine, and probably therefore of quinine, lessen the excitability of the muscles.

Abdominal Organs.—Upon the stomach and intestines quinia acts very much as a simple bitter. In moderate doses it stimulates digestion and increases the appetite; in large doses it not unfrequently causes nausea and vomiting. When there is any morbid irritability of the mucous membrane of the stomach or bowels, its irritant action is often very marked, and its continued use in large doses has been known to cause gastritis.

Many years since, M. Piorry asserted that a large dose of quinia would produce a distinct immediate lessening of the size of the spleen in cases of intermittent; but the testimony of very numerous observers to the contrary is so concurrent as to render the truth of his observation highly improbable. Several observers[*] have stated that the exposed spleen of an animal can be seen to contract when sulphate of quinia is injected into the stomach, veins, or cellular tissue; but other investigators[†] have failed in their attempts to produce this asserted contraction. The experiment necessitates such abnormal exposure of the organ that only a very pronounced and very constant diminution could establish the assertion that quinia produces contraction of the spleen, and our present knowledge indicates that the alkaloid has no immediate decided influence on the size of the organ.

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[*] M. Piorry, *Archives Générales de Médecine*, 1847; M. Pagès, *Gazette Médicale*, 1846; also Dr. Küchenmeister, *Archiv für Physiol. Heilkunde*, Bd. x.; M. Mosler, *Pathologie der Leukaemie*, Berlin, 1872, p. 451; Jerusalimsky (*Centralblatt Med. Wissen.*, 1876, p. 476). The latter observer believes the contraction to be caused chiefly by an action on the peripheral splenic nerves and muscles.

[†] Magendie (*Gaz. Méd.*, 1847), and especially L. T. Bochefontaine, *Recherches Expériment. à la Contractilité de la Rate*, Paris, 1873.

Organs of Circulation and Blood.—Briquet, who first studied closely the action of quinia upon the circulation, found that in large doses it lowers the arterial pressure in the lower animals. The experiments have been confirmed by various observers, notably by Schlockow (*De Chini Sulfavici*, etc., Bratisl, 1860), A. Eulenburg (*Reichert's Archiv*, 1865), and Cerna (*loc. cit.*, 194). It has been abundantly proven that the alkaloid thrown into the jugular vein, introduced into the coronary artery, or in any way brought in contact with the heart, lessens the force and frequency of the pulsations, and finally produces diastolic arrest; also, that this result is not influenced by separation of the mammalian heart from the nerve centres, and occurs in the cut-out frog's heart. In man, very large doses of quinia (thirty to sixty grains) lower the force and frequency of the pulse; a pulse-rate of forty has been noted, and in reported cases of quinia-poisoning the pulse has been imperceptible at the wrist. Under the latter circumstances the pulse-rate may be increased, but the cardiac force is reduced to a minimum. The evidence is conclusive that both in man and the lower animals quinine in sufficient amount is a powerful depressant to the heart-muscle or ganglia.*

Schroff (*Medizin Jahrbücher*, 1875) found that in the quinized animal neither galvanization of a sensitive nerve nor asphyxia was able to produce vascular contraction and rise of blood-pressure, and Jerusalimsky (*Centralb. Med. Wissensch.*, 1876, p. 476) asserts that in frogs dilatation of the vessels could be seen, so there is some reason for believing that toxic doses of quinia paralyze not only the heart, but also the vaso-motor system.† Both Schroff and Jerusalimsky noticed that the fall of arterial pressure produced by quinia is preceded by a rise of the pressure, accompanied with an increase of the cardiac action. This observation has been confirmed by G. Sée and Bochefontaine (*Compt.-Rend. Acad. Sci.*, T. xcvi. p. 267); but no observer seems to have shown that the rise of pressure is more than a temporary phenomenon. Sée and Bochefontaine affirm that the increased cardiac action continues some time after the pressure begins to fall. The primary rise of pressure may be the result of a stimulant action upon the vaso-motor centres, as Jerusalimsky found that it was not produced after division of the cord. Jerusalimsky attributes the increase in the pulse-rate to paralysis of the inhibitory apparatus, a view which is supported by the assertion of Cerna that previous section of the pneumogastric prevents the quickening of the pulse-rate.

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* Pantellejeff (*Centralb. Med. Wissensch.*, xviii., 1880, 529) states that atropia will cause the heart arrested by quinine to recommence its action.

† M. Chirone believes that by quinia the heart is arrested in *active* dilatation. The theory is very improbable. See *Rivista Clinica di Bologna*, abstracted in *Jour. Physiolog. Norm. et Patholog.*, 1876, p. 844.

Heubach, in a series of experiments on the influence of galvanization of a sensitive nerve upon the circulation after the exhibition of quinine, failed to prove any paralysant action of the drug, although in some of his experiments the reflex activity was paralyzed.

I have never been able to perceive any depressant action upon the circulation in man after ordinary therapeutic doses (three to five grains) of quinia, and I believe that in tonic doses quinia produces no perceptible sedation of the circulation, but that the largest antiperiodic doses have a distinct influence.[*]

According to Bonorn and Arvedi, to Magendie, to Monneret, to Melier, and to Baldwin, in animals killed with quinia the blood is found to be dark, defibrinated, fluid, and incapable of forming a clot. Briquet, however, denies that this alteration of the blood is constant or even common in quinia-poisoning, as he found it in only four out of twenty-three dogs so sacrificed; and he believes that it is merely an accident dependent upon the method of death. In a series of analyses, apparently carefully made, he found that the continued use of quinine augments the proportion of fibrin, but lowers that of the red corpuscles.

In 1867[†] Prof. Binz announced the fact that quinia added to human blood in the proportion of one part to four thousand immediately checks and in a short time arrests the amœboid movements of the white blood-cells. Confirmation of this has been furnished by Scharrenbroich (*Das Chinin als Antiphlogisticum*, Inaug. Dissert., Bonn, 1867), by Kerner (quoted in *London Practitioner*, vol. vii. p. 321), by Geltowsky (*London Practitioner*, vol. vii.), and by Jerusalimsky (*Centralb. Med. Wiss.*, 1876, p. 476). The minimum effective strength of the solution has been found to vary in different species of animals, and even in different individuals of the same species.

It is a matter of great interest to determine whether quinia acts in the living organism as on the stage of the microscope; and, to settle this point, Prof. Binz (*Virchow's Archiv*, Bd. xlvi., 1869, p. 138) has experimented according to the method of Cohnheim. He found that when the mesentery of curarized frogs to which quinia had been given was exposed upon the stage of the microscope, no accumulation of white blood-cells in the small vessels, or passage of them out into the tissues, occurred upon irritation; or, if after a time these phenomena commenced, they were at once checked by a small hypodermic injection of the alkaloid. When the inflammatory process had already commenced in a "Cohnheim frog," an injection of quinia would cause the wandering out of the corpuscles to cease, and would bring about a gradual clearing of the white cells from the choked-up vessels. Prof. Binz further took two young cats, and, after poisoning one of them with quinia, examined their blood. In the blood of the unpoisoned animal the white cells were far more abundant than in that of the poisoned cat. From these facts Prof. Binz deduces the conclusion that quinia acts destructively in the system upon the white blood-corpuscles, in the same way as when they are out of the body. Dr. Geo. R. Cutter (*Psychological and Medico-Legal Journal*, Feb. 1875) has experimentally confirmed the effect of quinia in preventing the extrusion of white blood-cells in the frog's mesentery, and A. Martin (*Das Chinin als Antiphlogisticum*, Inaug. Dissert., Giessen, 1868)* has not only done this, but has also found that the action of the drug is apparent in the centre of parenchymatous organs, such as the liver.

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[*] Some studies have been made upon the action of the drug on the capillaries of the brain, but the evidence is as yet contradictory and insufficient. Consult *Psychological and Medico-Legal Journal*, 1875, p. 33; also, *Archives of Medicine*, i. 33.

[†] *Archiv für Microscop. Anatomie*, iii., 1867. Consult, also, *Experimentelle Untersuchungen über das Wesen der Chininwirkung*, Berlin, 1868; *Virchow's Archiv*, Bd. xlvi., 1869, p. 137; *Berlin. Klinische Wochenschrift*, Nov. 1871.

On the other hand, Schwalbe† could detect no difference in the blood of a cat before and after poisoning by quinia; and the experiments of Geltowsky (*loc. cit.*) upon frogs and guinea-pigs have yielded similar results: in all cases after fatal poisoning by the alkaloid the movements of the corpuscles were found to be very active.

These results are in opposition not so much to the experiments as to the deductions of Prof. Binz,—deductions which seem to me scarcely warranted by his own investigations. The experiments which he performed in the Cohnheim method at most prove only that poisonous doses of quinia prevent or arrest inflammation. The local accumulation and the out-wandering of the blood-corpuscles are the result of a local inflammation or irritation, and if the quinia should in any way check this it would of course put an end to the phenomena mentioned. Again, quinia might, in the case of the cat, have lessened the proportion of blood-cells by checking their formation.

The exact nature of the action of the alkaloid upon the white blood-corpuscles in the body must, therefore, be considered undetermined, even when poisonous doses are used; when therapeutic doses are employed, the doubt is of course still stronger.

It would seem that quinia acts also upon other portions of the blood than the white corpuscles. Manassein (*Ueber die Dimensionen der rothen Blutkörperchen unter verschiedenen Verhältnissen*, Berlin, 1872) has found that in fever occurring in the lower animals the red corpuscles are diminished in size. If in this condition a decided dose of an antipyretic, such as quinia or alcohol, be given, and the temperature falls, the globules resume their normal size. That the change is due to the fall of the temperature rather than to a direct action of the drug is, I think, demonstrated by the fact of its occurrence whenever the fever-heat is lowered by the application of external cold. The experiments of Manassein, therefore, do not prove that quinia exerts any direct action on the red corpuscles. The investigations of Binz

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* Quoted by Binz, *Virchow's Archiv*, Bd. xlvi. p. 137.

† Quoted by Kerner, *Pflüger's Archiv*, Bd. i. p. 203.

(*Archiv für Experimentelle Pathologie und Pharmakologie*, Bd. i., erstes Heft, 1873), however, appear to show that the alkaloid lessens the ozonizing power of the blood; for he found that in young cats, to which he had given a very large but not fatal dose of quinia, the freshly-drawn blood affected the tincture of guaiac much less than it normally should.

When blood is drawn from the body and allowed to stand, acid is developed in it. Zunst (*Beiträge zur Physiologie des Blutes*, Inaug. Dissert., Bonn, 1868), who has studied this subject most closely, divides the investigation into—study of the production of acid in the time from the escape of the blood from the vein to its coagulation, and study of the slow changes which increase its acidity when coagulated until putrefaction has fairly set in. Prof. Binz believes that this development of acid is due to oxidation, and by an elaborate series of experiments has determined that quinia (also sulphate of bebeeria and picrate of sodium in almost as great degree) inhibits these changes very greatly in both their varieties. These experiments are in accord with the previous ones of A. Schulte (*Centralblatt für die Medicin. Wissenschaften.* Nov. 1871); the facts may, therefore, be considered proven.

If ozonized oil of turpentine be dropped into an alcoholic solution of guaiac resin, no alteration of color occurs; but if a drop of blood be added, the blue appears at once: *i.e.*, the blood acts as a carrier of ozone from the turpentine to the resin. Prof. Binz has found that quinia, even in so small an amount as one part in twenty thousand, has a perceptible influence in preventing this. Similarly, when into a dilute watery solution of the sulphate of indigo carbonate of sodium is thrown until the reaction is decidedly alkaline, and a little blood, and subsequently ten drops of ozonized turpentine, are added, a green color begins at once to develop, and in a little while passes into the clear yellow of isatin. In this case also the blood acts as a carrier of ozone, and Binz and his pupil Ransoné (*Ueber einige Beziehungen des Chinin zum Blut*, Inaug. Dissert., Bonn, 1871) have found that quinia also inhibits this action, one part of it added to a thousand of the mixture delaying the change of color for an hour. In these experiments Binz used a large number of different salts of quinia, and found that they acted identically. That the action of the alkaloid was on the blood, not on the indigo and guaiac solutions, was shown by the fact that when similar solutions without the blood were shaken in the air and absorbed ozone, the characteristic colorations of its action were produced just as readily when quinia was absent as when it was present. Binz also proved that the red corpuscles were the portions of the blood affected. On adding crystallized hæmoglobin from horses' blood to the guaiac solution he found that it acted as an ozone-bearer between the turpentine and the guaiac, and further demonstrated that quinia had the power of preventing this action.

As it is established that quinia exerts a decided antipyretic action (see p. 71) in ordinary fever, it is an exceedingly plausible theory that the lowering of temperature is due to a checking of the ozonizing power of the blood. To attribute, however, the general medical virtues of quinia to an action on the white corpuscles seems to me unreasonable; for from the experiments of Prof. Binz himself upon the lower organisms it would appear that quinine acts upon all animal germinal matter; and it is probable that the protoplasm of the nervous system, being more specialized than that of the white corpuscles, would be more susceptible of the influence of the alkaloid. Prof. Binz states that both conine and camphor act more forcibly upon the white corpuscles out of the body than does quinine, and Dr. T. Lauder Brunton and Theo. Cash have found that morphine, veratrine, and codeine check the ozonizing power of the blood; whilst digitaline, picrotoxine, and caffein increase it. Each of these principles has its own peculiar physiological action, differing from that of quinine and the other alkaloids (*St. Bartholomew's Hosp. Rep.*, xviii. 269). It seems, therefore, to me absurd to attribute such diverse physiological actions to the one common property of the group, and I think that we must consider the antozonizing power of quinine as simply one of its functions, and not as the basis of all its relations with the human organism.

Antiseptic Action.—As long ago as 1765, Dr. Pringle (*Observations on Diseases of the Army*, London, 1765) called attention to the fact that cinchona bark, in decoction or powder, has the power of preventing for a time putrefaction in flesh; and more recently the subject has been studied by Mayer, by Pavisi, by Hallier (*Das Cholera-Contagium*, Leipsic, 1867), by Herbst, by Polli, and especially by Binz (*Virchow's Archiv*, Bd. xlvi., 1869, p. 68; and *Untersuchungen über das Wesen der Chininwirkung*, p. 20), to whose elaborate articles I must refer my readers for details and references. The experiments of these authorities have demonstrated that quinia in the proportion of one part to three hundred will preserve for a long time flesh, meal, milk, butter, urine, albumen, etc., and will check very markedly the alcoholic fermentation in honey or in syrup. Prof. Binz has demonstrated that this antiseptic action is due to a poisonous influence exerted by the quinia upon the fungi which are the immediate cause of the changes. According to his experiments, the larger infusoria, such as Paramecia and Colpoda, are killed by a solution of quinia of the strength of one in eight hundred immediately, of one in one thousand after some minutes, of one in twenty thousand after some hours. Upon the ordinary mould Penicillium, upon Vibrios and Bacteria, as well as upon the higher infusoria, quinia acts with a similar fatality. In the case of the Vibrios and Bacteria a decidedly stronger solution than the one mentioned is required to quiet movement. Bochefontaine (*Archives de Physiologie*, July, 1873) found that a solution of one per cent. was needed for a vigorous rapid action, and that some active granules could even be found in it after three days. According to Binz, the singularity of the influence of quinia is shown by the fact that a solution of salicin, in the proportion of one part to forty, does not kill Paramecia and Colpoda. Indeed, these infusoria were not even affected by this strong solution of salicin, and they endured a solution of morphia of one part to one hundred and twenty for an hour, and a five per cent. solution of strychnine for some minutes. Although fungi will appear after a time in ordinary solution of the sulphate of quinia, I think it must be considered well established that this and other salts of the alkaloid are extremely poisonous to the fungi of putrefaction and of other ordinary fermentations.

Uterus.—In 1871, Dr. Monteverdi announced (*Annales et Bulletin de la Société de Médecine de Gand*, May, 1871) that quinia is a uterine stimulant, causing at times in the gravid womb contractions sufficiently violent to induce abortion, and, when given during labor, intensifying greatly the uterine pains, and after labor causing rapid expulsion of the placenta and arresting uterine hemorrhage; affirming, further, that in amenorrhœa or in menorrhagia from uterine inertia its action is no less marked. Although this has been received as new the world over, so long ago as 1855 Dr. John S. Wilson (*Southern Medical and Surgical Journal*, p. 341, 1855) called attention to the uterine action of quinine, and in 1860 reasserted his belief (*Southern Journal of Medicine*, Sept. 1860), which in the mean while had been confirmed by Dr. J. H. Rich in the *Charleston Medical Journal and Review;* and in 1858 Dr. Jos. J. West (*Savannah Journal of Medicine*, vol. i. p. 19) wrote, "Many regard the use of quinine as dangerous and even criminal in any diseases in pregnant women. The belief of these persons is that this substance exercises a direct influence upon the uterus, *causing powerful contractions* and expulsion of the fœtus. And to support this notion they are ready to bring forward innumerable instances of abortion after its use,—of cases of sudden suppression relieved by a prompt use of the same remedy." He then goes on to say that these abortions, etc., were due to the intermittent fever and not to the drug. Surely this is enough to show that the oxytocic action of quinia was believed in many years ago by numbers of our Southern practitioners. The question now is whether the drug has any such action. It is evident that the answer to this should be made out in three different ways. First, Is there any evidence of quinia producing abortion in healthy women or in females of other animals? Second, How strong is the evidence of its producing abortion in women suffering from ague? Third, What is the evidence in regard to the action of quinia during labor?

In regard to the first of these sub-questions, the only affirmative evidence I have met with is in the experiments of M. Rancillia (*L'Union Médicale*, 1873), who saw abortion in two bitches follow the administration of from six to nine grains of quinia: as the pups in one case were already dead before the administration of the drug, it would seem that this investigation was not on such a scale as to be at all conclusive. Moreover, I have given quinia to two pregnant cats, in one case in sufficient quantity to cause death, without disturbing the products of conception. On the other hand, I have met with no evidence that quinia is capable of inducing abortion in healthy pregnant women. Dr. Sayre's case (*American Practitioner*, 1871, p. 260) is certainly no proof whatever that quinia will originate labor, as labor had commenced under the influence of the hot and cold douche and other measures employed *before* the quinine was given. Prof. Chiara, of Milan, has furnished (*L' Union Médicale*, Nov. 20, 1873) very strong evidence that quinia is incapable of originating uterine contractions in healthy pregnant women. In his public service, two doses of a gramme (15.34 grains) each were given without effect daily for two successive days to eight women all in the eighth month of pregnancy. It being necessary to cause abortion, one gramme was given daily to one woman for seven days, to another for three days, without in either instance any effect, so that the labor had to be brought on in the usual manner. On the whole, I believe that the first question must at present be answered in the negative.

In answer to the second sub-question, some evidence has already been adduced to show that abortion may be so caused. To it may be added the assertion of Dr. Walraven (*Boston Medical and Surgical Journal*, 1873) that he has frequently seen the exhibition of quinia followed by abortion, the record of two cases of such character by Dr. Burt (*Medical and Surgical Reporter*, 1870), and no doubt the affirmations of others which I have not seen. Opposed to this, however, is the overwhelming fact that the great body of the profession have for centuries been giving quinia in one form or other to pregnant women indiscriminately, and if abortion had been produced it must have been noted long ago. Further direct testimony is not wanting. Malaria often induces abortion, and Dr. Erwin (*St. Louis Medical and Surgical Journal*, March, 1872), Dr. Jas. C. Harris (*American Practitioner*, April, 1872), and Dr. A. Russwurm (*American Practitioner*, 1871, No. 4, p. 127) testify from personal experience that quinia will arrest abortion from such cause. Dr. J. A. Ashford (*National Medical Journal*, Oct. 1871), Dr. Beauchamp (*American Practitioner*, 1870), Dr. Rooker (*Ibid.*), Dr. J. S. May (*Ibid.*), and Dr. A. d'Arcourd (*Medical News and Library*, May, 1873), have given the alkaloid to hundreds of pregnant women in large doses without result. Other testimony might be adduced; but it seems to me incredible, in the face of daily experience, that even the largest therapeutic doses of quinia are abortifacient in malarial fevers or in health.

In regard to the third sub-question, at the time of the writing of the third edition, the evidence, although greatly preponderating in one direction, was scarcely sufficient to be decisive.* At present, it seems established that quinine in full doses (ten to twenty grains) is a very powerful stimulant to the uterine contractions during labor. The pains it produces so exactly simulate the natural ones as to indicate that they are not so much caused by a specific action of the drug, as by its arousing the general nervous forces of the system. Be this as it may, most of the leading accoucheurs of this city and of New York are accustomed to rely upon quinine in cases of uterine inertia from exhaustion.

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* For details of the evidence the reader is referred to the third edition. Consult also *London Practitioner*, xvii., xviii., xix.

Kidneys and Elimination.—The manner in which quinine finds entrance into the blood has been especially studied by Dr. Kerner (*loc. cit.*). As the gastric juice is very acid, it is evident that the alkaloid will be rapidly dissolved in the stomach and be put into the conditions most favorable for its absorption: if, however, the salt of quinia escape from the stomach into the intestines, it will be liable to be precipitated by the alkaline juices, as well as by the bile, whose acids form very insoluble salts with it. The presumption is therefore strong that, when gastric absorption fails to take place, at least a portion of the quinia will pass out with the fæces. That this actually does occur has been proven by Kerner and others, who have found the alkaloid in the excrement of persons taking it. As the blood is alkaline, it would appear probable that the quinia salt so soon as entering it would be precipitated. That this does not occur, according to the researches of Kerner, is due to the solvent power of the gases contained in normal blood.

The authority mentioned found that one thousand parts of blood which was defibrinated and deprived of its gases, at a temperature of 36° C. dissolved in an hour only 0.398 part of pure quinia. Water saturated with carbonic acid gas dissolves the sulphate of quinia pretty freely; and Kerner also experimentally determined that when a neutral solution of a salt of quinia is added to a very dilute solution of carbonate of sodium no precipitate occurs. It would appear, then, that the quinia is held in solution in the blood by reason of the loosely-combined carbonic acid gas in that fluid.

It has been proven by the analyses of Landerer (*Repertorium für Pharmacie*, Bd. xxv., 1836), of Dietl (*Wiener Medizinische Wochenschrift*, 1852), of Briquet (*loc. cit.*), of Binz, and of De Renzi (*Bull. Thérap.*, xci. p. 45), that quinine escapes from the body through the kidneys. According to Briquet, it may generally be found in the urine half an hour after the administration of a large dose. Its removal, according to the researches of Binz, goes on slowly, for it is stated (*loc. cit.*, p. 167) that in six experiments only a little more than two-thirds of the ingested quantity was excreted in the first forty-eight hours. Further, De Renzi, Yvon, and Dietl (*Die Pflanzenstoffe*, 1883, 1443) have found it in the urine six or seven days after the ingestion of the last dose. Dr. L. Thau, however, in three experiments, out of the 4.4586 grammes of the alkaloid which were given, recovered from the urine passed during the forty-eight hours 4.3 grammes, so that only 0.1586 gramme remained unaccounted for. A portion of this residue was perhaps lost in the chemical operations; but it is probable that some of the quinine is eliminated through other channels than the kidneys, since Prof. Binz has found it in the saliva of a poisoned dog, and Landerer (*Buchner's Repertorium*, 1839 and 1842) states that he has detected it in the urine, sweat, tears, milk of nursing women, and in the serum of dropsical effusions, whilst Albertoni and Rienzi find it abundant in the bile when it has been taken by the mouth, but not when it has been given hypodermically. Dr. Thau determined that from a third to somewhat less than half of the ingested quinine escapes from the body in the first six hours, and that in the first twelve hours about three-fourths are excreted.[*] Welitschkowski found (*St. Petersb. Med. Wochenschrift*, 1876) an elimination of sixty-five per cent. the first day and twenty-five per cent. the second day. Prior gives the second day as the usual final limit of elimination. I think we may consider that after a few doses the alkaloid is practically eliminated in forty-eight hours; but that when it has been given continuously, or kidney-disease or great feebleness of circulation exist, the system may contain a notable amount of the quinine for a longer period. The researches of Welitschkowski are in accord with those of Jürgensen and Thau in showing that in cardiac and renal disease and in low fevers elimination proceeds very slowly, more of the alkaloid being thrown off in the second than in the first six hours after its ingestion.

Ranke was, I believe, the first to notice that quinine produced a great decrease in the elimination of uric acid. This was confirmed by H. V. Bosse (*Inaug. Diss.*, Dorpat, 1862), and by Dr. G. Kerner (*Pflüger's Archiv*, 1870, iii. 93). The latter observer found, when about nine grains of quinine were taken in divided doses during the course of the day, the urea was decreased not quite one-eighth, the uric acid to a little less than one-half, the kreatinine was slightly increased, and the nitrogenous material decreased about one-ninth. When a very large dose (thirty-eight grains) was taken in the morning, the urea and the kreatinine were each decreased about one-fourth, as was also the collective nitrogenous material; the phosphoric acid was lessened about one-fifth, and the uric acid about four-fifths. Zuntz (quoted by G. Strassburg, *Archiv für Exper. Path.*, Bd. ii. p. 343) found that twenty-five grains of quinine reduced his elimination of urea nearly forty per cent. A. Schulte also found 1.8 gramme quinine depress the elimination by the kidneys thirty-nine per cent. (*Inaug. Diss.*, Bonn, 1870); yet in the experiments of Unruh (*Virchow's Archiv*, 1869, xlviii. 227) the alkaloid usually, but not always, acted in this way, and in the trials of H. Oppenheim (*Pflüger's Archiv*, 1880, xxxiii. 446) the excretion of urea was actually increased. Nevertheless, the experiments, upon the dog, of Rabuteau (*Bulletin Thérapeutique*, t. lxxv. p. 475) and of Hermann von Boeck (*Untersuchungen über die Zersetzung des Eiweisses im*

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[*] Dr. G. Kerner (*Pflüger's Archiv für Physiologie*, 1870) asserts that the quinia as excreted is in an amorphous, uncrystallizable form. He also has discovered in the urine of persons taking quinia a peculiar substance, sometimes amorphous, sometimes in acicular prismatic crystals, free from bitter taste, possessing the quinia inflorescence, which he believes to be a derivative formed in the body from the ingested alkaloid. He has not been able to get this substance in such quantity as to analyze it or further examine it, but has produced a principle (*dihydroxyle quinia*) which he believes to be identical with it by acting on quinia with the permanganate of potassium. An elaborate series of experiments have shown that the dihydroxyle quinia is physiologically inert. This dihydroxyle quinia must be produced in small amount, if at all, as there is abundant evidence that quinia is largely excreted as quinia (see *Ph. Jour. and Trans.*, ix. 125).

Thierkörper, Munich, 1871), bear strong evidence to the fact that quinine does decrease the elimination of urea; and the recent very elaborate studies of Dr. Prior (*Pflüger's Archiv*, Bd. xxxiv. 237) warrant us in believing it established that quinine powerfully depresses the elimination of the nitrogenous excretory principles. That such decrease is due to diminished formation and not to lessened elimination seems proven by the fact that in Prior's experiments there was no increase of nitrogenous excretion beyond the norm following the omission of the quinine. The conclusion seems logically inevitable that quinine has *a direct or indirect influence upon the tissue-changes of the human organism.* Contrary to what might have been expected, Strassburg (*loc. cit.*), in an elaborate series of experiments, found that quinine had no very decided effect upon the elimination of carbonic acid either in healthy or in fevered rabbits.

THERAPEUTICS.—At present our estimate of the value of quinia in disease, and our knowledge of its therapeutic use, rest solely upon clinical observation. We are not as yet able to apply what information we have of its physiological action, nor, indeed, are we even able to explain its known clinical action by its observed effects on the healthy organism.

On account of its power of arresting or preventing putrefactive fermentation by killing the microscopic entities which produce such changes, Prof. Binz has recommended it in the so-called *septic diseases*. The chief evidence which he produces is in some ten experiments made upon dogs and rabbits. In each of these experiments two similar animals were poisoned with putrescent liquids, and to one of the pair quinine was freely administered. In two cases the cinchonized animal recovered, whilst its fellow perished; in three experiments neither of the animals died; and in the other five trials the cinchonized animal lived from two to twenty-four hours longer than the other. These experiments are certainly too few and indecisive to prove in any degree Prof. Binz's view. To my mind they indicate very strongly that quinia has no such influence over the disease as he claims for it. If living germs in the blood were really the cause of the septic symptoms, and quinia killed such germs, its action would be as manifest and as unmistakable as it is in intermittent fever. The results of Prof. Binz's experiments indicate no such specific action, but rather that the quinia in such cases does good by sustaining the nervous system, or in some other unknown manner. In *pyæmia* in man, quinia has been frequently employed, but exerts no specific action.

It has not, that I know of, been proven that therapeutic doses of quinia lower, to any marked extent, animal temperature in the healthy man. Dr. G. Kerner and Dr. Jürgensen have each noticed that full doses of quinia appear in a healthy man not to affect sensibly the temperature, but to prevent the rise which normally occurs from exercise. Thus, in Kerner's experiment, certain gymnastic exercises, which when performed in his ordinary state elevated his bodily temperature 2° C., affected the latter to the extent only of 0.2° to 0.35° C. when quinia was freely exhibited.

Even Dr. C. Liebermeister (*Deutsches Archiv für Klinische Medicin*, Bd. iii., 1867) acknowledges that numerous experiments have shown him that the alkaloid has no constant action on the bodily heat in health, and details a case in which forty grains administered within seven hours caused no depression of temperature. The same authority claims, however, that by a very large number of experiments he has demonstrated its power of lessening fever-heat. In one hundred and seventy-eight observations in *typhoid fever*, twenty grains of the quinine having been given during the night, the morning temperature was lower than that of the previous evening by, on the average, 1.63° C. On one hundred and seventy-six different occasions a scruple of quinine was given during the day; sixty-nine times the temperature was lower in the evening than in the morning, ten times it was the same as in the morning, and ninety-seven times it was higher than in the morning. A committee appointed by the London Clinical Society (*Transactions*, vol. iii., 1870, p. 201) experimented with the drug on about fifty cases of various diseases. They assert that the antipyretic action of large doses was very decided, appearing within from one to two hours after the exhibition of the drug, and lasting from a few to many hours. In a very recent publication Liebermeister asserts that he has given some ten thousand doses of quinine as an antipyretic and has almost unbounded confidence in it. He insists that from twenty to forty-five grains must be *given within the hour*, and not repeated oftener than once in twenty-four or forty-eight hours.

Naunyn and Quincke (*Reichert's Archiv für Anatomie*, 1869) found that sometimes quinia prevented the development of fever after the division of the spinal cord in animals, but in other cases failed to do so. Binz (*London Practitioner*, p. 4, 1870) has achieved similar results: he says that if the conditions of the fever are too favorably constituted the effect of the quinine fails thoroughly. The drift of our present clinical evidence seems to indicate that quinia exerts in febrile disease a decided antipyretic action, which is especially manifested during those stages of disease in which the natural tendency is towards a lowering of temperature. In *typhus* and *typhoid fever*, *scarlatina*, severe *erysipelas*, *rheumatic hyperexia*, etc., after the use of the cold bath (see Part II.) twenty grains of the alkaloid are often very efficacious in preventing a rapid return of the excessive fever. If the experiments spoken of above be correct, this reduction of temperature must be due to an action on the tissues and not on the central nervous system. It would seem, however, more probable that quinia acts as an antipyretic by stimulating the inhibitory chemical centre; but decision of this must be reserved for future investigations. As an *antipyretic* the drug should be used whenever there is serious elevation of temperature, except it be in cases of simple inflammation of the brain or its membranes. All antipyretic remedies appear to act more strongly on children than on adults; and accordingly Dr. Rapmund (*Deutsches Klinik*, 1874, p. 51) has found quinia of the utmost service in serious diseases of children with high temperature, especially *lobular pneumonia*. Much of the failure which has hitherto attended its employment undoubtedly has been due to a faulty method of administration.

As a simple tonic, quinia is used by every one; but I have never been able to see that the ordinary combination of it with iron is of much more value in simple cases of debility than iron with quassia or other simple bitter; but if, as is probable, it be true that quinia lessens to a very great extent the elimination of nitrogen, *i.e.*, the consumption of tissue, the general practice has a good foundation.

When given in very large doses, quinia, as has been already shown, acts as a powerful depressant, and as such has been used by Briquet and other French physicians in *rheumatism*. As much as sixty or seventy grains a day have been given, and it is beyond dispute that under the influence of these heroic doses the symptoms of inflammatory rheumatism have often rapidly abated; but the method has found little favor out of France, and is less efficient and more dangerous than other plans of treatment now in vogue.

In *inflammatory rheumatism*, after the acute symptoms have abated, when the patient shows evident signs of weakness, especially if there be profuse sweating during sleep, fifteen grains of quinine daily are often of great service.

Various theories have been brought forward to account for the wonderful power quinia has upon all forms of *malarial disease;* but, as we know nothing of the nature of malaria or of the method of its action, and as we are very partially informed as to the effects of quinia upon the healthy organism, it seems to me perfectly futile to endeavor to explain why it averts a paroxysm of intermittent. I shall not, therefore, occupy space with such discussion. The present seems, however, the fitting place to notice the discovery of Dr. H. Bence Jones in regard to the existence of a body similar to quinia in the animal organism.

Quinia and its salts have the remarkable property of converting the chemical rays of the spectrum into light, or, in other words, of rendering visible the ordinary invisible rays of the solar or other spectrum. Connected with this fact is probably the phenomenon known as the fluorescence of quinia. When a colorless watery solution of one of its salts is examined, a pale-blue line upon the surface is very noticeable; and Prof. Stokes has shown that solution of quinia has the power of entirely stopping certain of the rays of light, so that when a beam is transmitted through it to light up a second vessel of the solution this latter displays no fluorescence. Dr. H. Bence Jones (*Lectures on Pathology and Therapeutics*, London, 1867) has found that when the electric light is used this test is so delicate that one grain of the alkaloid may be detected in 1,450,000 grains of water. He has also discovered that man and animals are pervaded by a substance which, in its action on light and in many chemical reactions, very closely resembles, if it be not identical with, quinia. Believing this substance to be probably an alkaloid, he has given it the name of *animal quinoidine*. Drs. Edward Rhoads and William Pepper, Jr. (*Pennsylvania Hospital Reports*, vol. i., 1868), have made observations upon ten cases of malarial fevers in which no quinine had been used, and have found the fluorescence of the blood to be from 0 to 1½, instead of from 3 to 6, which is said to be normal. The significance of these results is at once apparent; but, before sufficient grounds shall have been obtained upon which to build a theory, far more extended researches on the variance of the fluorescence in health and in diseases other than malarial are necessary. Especially is this the case since Dr. Chalvet (*Schmidt's Jahrbücher*, Bd. cxli. p. 152, from *Gazette Hebdomadaire*, 2d series, t. v., 1868) has found that this fluorescent body exists in various foods and even in wine, and is therefore probably not of animal but of vegetable origin.

Quinia in its relations to *malarial fever* may be considered first as a prophylactic, secondly as a curative agent.

The value of the daily use of quinia to persons exposed to a malarial atmosphere has now been thoroughly tested in all portions of the world. In North and South America, in Europe, in Africa, in India, the prophylactic powers of quinia have been tried on the largest scale in connection with the military and naval services, and the testimony is unanimous in favor of the drug. A single citation will serve to illustrate this fact.* Dr. J. B. Hamilton (*Indian Medical Gazette*, Nov. 1, 1873) reports the case of a battery of one hundred and thirty-five men, quartered at Jubbulpore, East Indies, in the same barracks with an infantry regiment. Each of the artillerists received three grains of quinine every other day; to the infantry none was given. The result was that whilst three hundred out of the five hundred men of the regiment were sick at one time with malarial disease, at no period was more than four per cent. of the battery affected. The dose of quinia as a prophylactic may be considered as three grains a day, or possibly, in very deadly climates, three grains in the morning and two in the evening.

In *intermittent fever*, when there is sufficient time, it may be well to precede the quinia by a mercurial or other purge. If the expected paroxysm be so near that there is not sufficient time for the action of the purgative, the antiperiodic should be administered without previous preparation of the patient. The value of purgatives in obstinate intermittents, as an adjuvant to quinia, is often overlooked, although in some cases the employment of purgatives, and of such diuretics as cream of tartar, seems to be almost essential for the successful use of quinia.

When there is necessity for prompt action, the antiperiodic may be given in a single dose, or in any other method that the circumstances of the case will allow; but ordinarily the best plan is to commence the exhibition of the drug about eight hours before the expected paroxysm, and to continue in hourly doses until from three to four hours before the attack is due.

In *pernicious fever*, or *malignant malarial* poisoning, no time should be lost after the first paroxysm in getting the patient cinchonized, as it may be uncertain whether the attack be of the quotidian or tertian type. At least thirty-five grains of the alkaloidal salt should be administered during the first twenty-four hours of intermission, and twenty-five grains during the second; in very severe types of the disease much larger doses even than these are necessary, less than fifty grains of the drug sometimes appearing to do but little good.

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* See also K. M. Downie, M.B., *Indian Medical Journal*, March 1, 1872.

In *remittent* or *bilious fever* it may often be advisable to give purgatives and febrifuges, but it is not proper to delay the exhibition of the antiperiodic on their account. As soon as the remission has appeared, the exhibition of quinia should be begun. Local inflammations or even severe cerebral symptoms occurring during a remittent fever are no contra-indications to the use of the specific. When gastritis exists, other channels of entrance than the stomach should be employed, on account of the local irritant action of quinia.

When the symptoms in remittent fever are severe and seemingly continuous, it may be not only proper, but necessary for the saving of life, to exhibit quinia freely during the period of fever. In large doses the alkaloid is probably antipyretic as well as antiperiodic, and I do not know of any theoretic or clinical objection to its use during the period of fever.

In *malarial intermittent neuralgia*, as in all other forms of abnormal manifestations of malarial disease, quinia is efficient, although it may be necessary to use it in large doses.

In *neuralgia* which, although not dependent upon malaria, assumes the intermittent type, quinia will often temporarily set aside the paroxysmal attacks, and sometimes effect a cure. The same fact may be stated in broad terms as true of *all non-malarial intermittent* affections. In the great majority of such cases, unfortunately, the action of the quinia is only temporary, and any controlling power is soon lost.

Various idiosyncrasies exist towards quinia. Prof. Karamitsas asserts that in some persons it causes hæmaturia (*Bull. Thérap.*, xcvii. 53): it not very rarely causes vesical irritation, and it is said that in some people (*Brit. Med. Jour.*, ii., 1869; *Berlin. Klin. Woch.*, 1877, 294; *Phila. Med. Times*, x. 166) a few grains given internally suffice to produce great œdema of the face and limbs, accompanied with a pronounced erythematous rash, in some cases closely resembling that of scarlatina (*N. Y. Med. Record*, xxi. 627), the whole subsiding in a few days with desquamation of the cuticle, even purpura, although with very doubtful correctness, has been ascribed to the alkaloid (*Boston Med. Surg. Journ.*, cix. p. 587). Chevallier describes (*Gaz. des Hôpitaux*, 1850) a peculiar affection of the skin, etc., as occurring among workers in bark.

Local Use of Quinia.—The effect of quinia upon the lower organisms has suggested its local use in various disorders *supposed* to depend upon the presence of such entities. Thus, Dr. Henke (*Deutsches Archiv für Klin. Med.*, Bd. xii. p. 630), finding some peculiar motile cells in the sputa of *whooping-cough*, employed inhalations of quinia with asserted good results. Dr. Henke was not, however, the first to suggest either this fungoid pathology of whooping-cough or the use of quinia. Prof. Binz in 1870 (*American Journal of Obstetrics and Diseases of Women*, iii.) claimed that quinia had a specific action in whooping-cough, provided it was given in large doses in solution, so as to come in contact with the mucous membrane in its passage through the pharynx; and in 1871 Letzerich (*Ibid.*, vol. iv. p. 761) announced that whooping-cough was due to a fungus in the lung. Prof. Dawson (*Ibid.*, 1873) has confirmed the value of the method of Prof. Binz; but, if the fungoid theory be—as I do not believe—true, the plan of Henke must certainly be the better one.

Again, Helmholtz recommended the local use of quinia in *hay fever*, believing that disease to be due to a fungus, and much testimony has been brought forward as to the value of the treatment. A weak, tepid solution (gr. j to iii—f℥i), as nearly neutral as possible, should be freely applied by snuffing it up, or, better, by means of Thudichum's douche. If the value of quinia in whooping-cough and in hay fever be established, it by no means follows that the theory which originated the use of the remedy is true. The alkaloid is certainly a stimulant to the mucous membranes, and in the later stages of *gonorrhœa* the topical employment of its solution (gr. v to x—f℥i) is often very serviceable.

ADMINISTRATION.—Owing to its bitter taste, sulphate of quinia is generally given in pill, which may be made with gum, or simply by adding a little sulphuric acid to the alkaloidal salt and quickly rubbing up the pasty mass into pills before it hardens. Whenever a rapid action is desired, the quinine should be given in powder, or in solution made by adding a drop of dilute sulphuric acid for every grain of the salt. In the use of pills of quinine, care should be exercised to see that they are soft and fresh, for when old and hard they not unfrequently pass through the bowels unchanged. The ready-made "sugar-coated" pills kept in the shops should be avoided, as uncertain in their action. The taste of the powder is best covered by chocolate or by liquorice.

When sulphate of quinia is given *hypodermically* it acts with much greater promptness and apparently with greater force than when administered by the stomach. Albertoni and Ciotto (*Bull. Thérap.*, xc., p. 403) found that when they injected it into the jugular vein it failed to appear in the bile, but when they administered it by the mouth it was freely eliminated with that secretion. Biliary salts of quinia are so insoluble that their re-absorption must be effected, if at all, very slowly; hence possibly the superior efficiency of the hypodermic method. The local irritant action of quinia, however, forbids its hypodermic employment, except in cases of great emergency. Given in this way, it very generally produces great local disturbance (abscesses, ulcers, etc.), and in several cases has caused fatal tetanus (*London Lancet*, 1876, i.). When it is so given, care should be taken to have *an excess of acid* (tartaric—the best) in the solution, to prevent precipitation of the quinine by the alkaline juices of the cellular tissue. The *bisulphate of quinine* (*Quininæ Bisulphas*, U.S.) is soluble in ten parts of water, and should be preferred for hypodermic use: even its solution should be slightly acidulated. Ten grains of quinine injected under the skin are probably equivalent to fifteen grains given by the mouth.

Contraindication.—On account of its irritant properties, quinine must be used with caution when there is irritability or inflammation of any part of the gastro-intestinal tract. It is strongly contraindicated by inflammation of the middle ear, and may greatly and permanently increase dulness of hearing. In connection with this is of great interest the statement of Dr. M. Friedmann (*Wien. Med. Presse*, 1884, 927) that ergotin, given with quinine or salicylic acid, greatly lessens the auditory disturbance.

The *hydrobromate of quinine* (*Quininæ Hydrobromas*, U. S.) is soluble in about 16 parts of water and in 3 parts of alcohol. It is stated that a ten per cent. solution in a mixture of alcohol, 25 parts, water, 75 parts, is not irritant when used hypodermically.

The *tannate of quinia*,* although not officinal, has been used to some extent, and is certainly not inefficient. It has the great advantage of not being disagreeable to the palate, but is less active and less certain than the more soluble salts of the alkaloid, and is also much slower in its operation. If given at all, it should be in doses one-third greater than those of the sulphate.

The physiological action of cinchonine closely resembles that of quinine, but seems not to be quite identical with it. Laborde states that pure quinine does not cause epileptiform convulsions in the lower animals, although commercial quinine does so on account of its impurity; and that in poisoning with cinchonine violent epileptiform convulsions are a chief symptom (*Compt.-Rend. Soc. Biolog.*, iv. 1882). M. Bochefontaine (*Comp.-Rend. Acad. Sci.*, T. xcvi. p. 503) affirms, however, that quinine does convulse, although less actively than does cinchonine, which latter alkaloid he found to vomit less than quinine. According to Johnnsen, the effect of cinchonine upon the elimination of urinary solids is even more powerful than that of quinine. It is eliminated unchanged, appearing in the urine in half an hour, and disappearing after massive doses only in ninety-six hours: the great bulk being thrown off in the first twenty-four hours (*Pflanzenstoffe*, 1480).

QUINIDINÆ SULPHAS. U. S.—*Sulphate of quinidine* occurs in long, shining, silky, acicular crystals, soluble in 130 parts of water at 62° F., in 16 parts at 212°; readily soluble in alcohol, nearly insoluble in ether. It is a basic salt, like the sulphate of quinia, readily taking another equivalent of acid. It behaves like its isomer with chlorine and ammonia, but is distinguished by rotating light powerfully to the right, instead of moderately to the left. It probably closely resembles quinine in its physiological and therapeutic properties, and is an efficient antiperiodic; the dose is about one-third larger than that of quinine.

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* For an elaborate discussion of the therapeutic value of this salt, see *Bulletin de l'Académie*, Paris, 1872.

Dextro quinia, a brown, amorphous substance, derived from chinoidine, is said to answer all the tests for quinia except to polarize to the right. It is probably an impure quinidia.

CINCHONINÆ SULPHAS—SULPHATE OF CINCHONINE. U. S.

The pure alkaloid cinchonia crystallizes in prisms and needles. The officinal *sulphate* of cinchonia is in short oblique prisms of a very bitter taste, soluble in fifty-four parts of water, more freely in boiling water, readily soluble in alcohol. From its solution in chlorine-water it is precipitated white by ammonia. Bill's test for it consists in adding the ferrocyanide of potassium in slight excess to its solution. A yellowish-white curdy precipitate is the result. On gently heating, this redissolves, but is again deposited, when the liquid cools, as abundant golden-yellow crystals.

Physiological Action.—Conzen (quoted by Husemann) has found that the action of cinchonine on infusoria and on fermentation is similar to but weaker than that of its sister alkaloid, and that on the movements of the white blood-corpuscles its influence seems transient. In Bochefontaine's experiments the relative strength of cinchonine to quinine was about 10 to 16 (*Ibid.*, p. 506; in Bernatzik's (on dogs only) as 4 to 5.

Therapeutics.—As an antiperiodic, cinchonia exerts a similar influence to quinia, but is probably about one-third weaker than that alkaloid, and must be used in correspondingly larger dose. Dr. J. B. Hamilton (*loc. cit.*) affirms as the result of experiment that cinchonia as a prophylactic against malaria is even superior to quinia. As a tonic I have never been able to perceive that cinchonia acts differently from quinia.

Cinchonidinæ Sulphas. U. S.—*Sulphate of cinchonidine* occurs in white, silky, lustrous needles or prisms, odorless, of a very bitter taste, soluble in 100 parts of water, freely soluble in acidulated solutions. It polarizes to the left, and is not fluorescent. G. Sée and M. Bochefontaine found that the lethal dose of cinchonidine for the frog is 0.015 gramme; for the dog, 2.50 gramme. The symptoms in the dog are general feebleness, titubation, increase of pulse-rate and arterial pressure, vomiting, salivation, convulsions,—less severe than those caused by quinine,—great loss of muscular power, stupor, fall of arterial pressure and of temperature, death from arrest of respiration (*La France Méd.*, 1883, 527). A boy, aged five years, took one hundred and twenty-eight grains in solution during six hours without vomiting. There were then convulsions, followed by great collapse, fall of temperature, pulselessness (with seventy-four cardiac beats per minute), dilated pupils, muscular relaxation, and, finally, death; consciousness being preserved to the end (*N. Y. Med. Journ.*, xxxix. 1884). It is evident that this alkaloid closely resembles its congeneric alkaloids in its action upon the human organism. Clinical experience has proven it to be a reliable tonic and antiperiodic. According to Byasson, it is eliminated by the kidneys unchanged. It has been claimed that it produces less disagreeable symptoms, both gastric and cerebral, than does quinine; but Dr. Rafferty, who has administered three hundred ounces of the sulphate, affirms that it is more apt to cause nausea and vomiting. The dose is one-third greater than that of quinine.

CHINOIDINUM. U. S.—*Chinoidin*, or *Quinoidin*, is a blackish substance, with an almost resinous fracture, which is obtained by the evaporation of the mother-liquor after the crystallization of the alkaloids out of it. This substance contains probably amorphous quinine and cinchonine, besides quinidine and cinchonidine. It is an excellent tonic and antiperiodic, and, on account of its cheapness, is largely used in some of the eleemosynary institutions of this city. It should be administered in about double the dose of quinine, and is most efficient in solution, but, on account of its taste, is often given in pills. Its solution should be made with acetic acid and water, aromatics being freely added, as it is apt to cause nausea.

The U. S. Pharmacopœia recognizes for use as a tonic an infusion of bark (*Infusum Cinchonæ*—1 to 16.6), dose, a wineglassful; a *tincture* of the yellow bark (*Tinctura Cinchonæ*—1 to 5), dose, one to two teaspoonfuls; a *compound tincture* (*Tinctura Cinchonæ Composita—Huxham's Tincture*), which, as a tonic, is the best preparation of the bark, and is a very elegant remedy in convalescence, in doses of one teaspoonful to a tablespoonful; and also a *fluid extract* and a *solid extract* (*Extractum Cinchonæ Fluidum* and *Extractum Cinchonæ*), the doses of which are five to fifteen drops or grains respectively.

ACIDUM PICRUM*—PICRIC ACID.

Picric or *Carbazotic Acid* is not officinal, but has been used to some extent in medicine. It occurs in pale, yellow, shining scales, but is employed by the therapeutist only in the form of a salt, on account of the deleterious influence of the pure acid on the gastric mucous membrane: the picrate of potassium, of sodium, or of ammonium may be used; but the last is the one generally chosen.

PHYSIOLOGICAL ACTION.—The only detailed study of picric acid known to me is that of Dr. W. Erb (*Die Pikrinsäure*, Würzburg, 1865). This observer found that the daily use of a grain (for ninety days) of a picrate produced, in a rabbit, yellowness of the conjunctiva, of the inner surface of the ear, and of the urine, with an occasional slight diarrhœa and great loss of weight, without any elevation of temperature. After a time the animal seemed to grow accustomed to the remedy, so as to regain in great measure its flesh. Three grains a day caused, in about two weeks, the death of the rabbit with symptoms of inanition. All the tissues, except the nervous, were stained of an intense reddish-yellow color, as was also the urine. Eight grains produced falling temperature, weakness, diarrhœa, collapse, and death, sometimes preceded by tremblings and even convulsions, in about twenty-three hours. Most of the tissues were stained yellowish-red. The most remarkable physiological effect of the poison occurred in the blood. The blood of animals slowly killed by a picrate was of a dirty-brown color, with distinct nuclei both in the red blood-disks and floating free in the serum. M. Erb found that this alteration in the corpuscles occurred during life and was accompanied by a decided increase in the number of the white corpuscles. These alterations in the blood were apparently the cause of death, and seem to have been due, so far at least as concerned the red disks, to a direct action of the poison upon the blood; for Erb found that identical or very similar alterations occurred in these corpuscles when the blood was mixed with the picrate of sodium outside of the body.

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* Picric Acid does not really belong in this chapter, but, as it has attracted most attention as an antiperiodic, in the ignorance which exists as to its physiological action, I have introduced it.

Erb found picric acid to act on man as on the lower animals. Twenty-four hours after the ingestion of fifteen grains of it the yellow color was very plain in the conjunctiva, the skin, and the urine. The temperature was not elevated, and gastric disturbance was usually absent, but sometimes it was severe. As with animals, so in man, picric acid was found abundantly in the urine. A teaspoonful produced no more violent symptoms in a man than bad vomiting and purging (*Wiener Med. Presse*, xxiii. 1526).

Prof. Binz (*Virchow's Archiv*, Bd. xlvi. p. 130) has found that picric acid exerts upon the infusoria an influence similar to, but much feebler than, that of quinia.

THERAPEUTICS.—The carbazotate of ammonium has been strongly recommended by various authorities in malarial disorders; but in the experiments of Erb the result was so negative that the possession of any antiperiodic powers by the drug is doubtful.* As an *anthelmintic*, the picrate has also been commended; but Erb found it powerless in cases of *tænia*, and for the destruction of the round-worm and thread-worm there is an abundance of safer and even more efficient remedies. A matter of the gravest importance is the asserted efficiency of the remedy in *trichiniasis*. Erb has produced slow poisoning with a picrate in rabbits which had been fed upon affected meat, and, on examining their bodies after death, found the trichina everywhere, even in the walls of the intestines, in very active life. On the whole, the testimony so far seems to indicate that picric acid has no value as a therapeutic agent. Erb affirms that in robust adults from nine to fifteen grains a day may be given for a long time with safety; but I would fear the effects of more than half that quantity.

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* Consult *Deutsches Klinik*, 1855, No. 40; *Medical Times and Gazette*, Sept. 1862; *New Remedies*, 1873; *Gazette des Hôpitaux*, xlv. p. 116; *Ohio Medical Recorder*, 1877.

AROMATICS.

There are certain remedies usually spoken of in treatises on Materia Medica under the general head of tonics, which might more properly be considered local stimulants, acting, as employed in medicine, upon the alimentary canal. These are the so-called aromatics, substances dependent for their virtues upon the presence of a volatile oil.

The volatile oils are essentially local irritants, causing when taken into the mouth intense burning pain; when confined upon the skin, rubefaction, blistering, and finally, if the contact be very prolonged, more destructive changes. Internally, taken in very large doses, they cause burning pain in the stomach, increased activity of the circulation, and a species of intoxication. In sufficiently large quantities they are irritant narcotic poisons. When administered in therapeutic doses they act almost exclusively upon the alimentary canal. As compared with that of the simple bitters, their influence is more powerful and more transient. They do not permanently increase the digestive power, but simply increase action for the time being. They are employed chiefly —to give pungency to bitter tonics; as *carminatives*, to stimulate the intestines to contract upon and expel flatus; to prevent the griping of purgatives; to disguise the taste of medicines, and to render nauseating drugs acceptable to the stomach; to act as condiments, and aid in the digestion of the food.

Injected into the circulation, the volatile oils lower the blood-pressure by depressing the heart's action, and even in comparatively small doses may cause immediate diastolic arrest. In this respect oil of cloves is one of the most powerful. The heart-action is undoubtedly direct and upon the heart itself: other muscular structures would seem to be similarly affected, as H. Kobert has found that the oil of mace directly lowers muscular excitability (*Arch. f. Exp. Path. und Therap.*, xv. 22).

Some of the tonic drugs containing a volatile oil also have in them a bitter principle which modifies their action. Such drugs may be known as *aromatic bitters;* as bitters they are less powerful than such drugs as quassia, and are especially indicated where the stomach is delicate and easily nauseated.

Inflammation of the stomach or bowels is the chief contra-indication to the use of aromatics. Unlike the simple bitters, they are often very useful in *diarrhœa* of nervous irritability or of relaxation, when no decided inflammation exists.

There is one property which is probably common to all the aromatic oils, and which may therefore be alluded to at this place with propriety,—viz., the power of producing local anæsthesia. In China the oil of peppermint has long been used locally in neuralgia; and my own experience with our native oil is in accord with that of Dr. A. Wright (*London Lancet*, 1874, ii.;

see, also, *Gaz. Méd.*, 1874) in finding it efficient in neuralgia and subacute rheumatism. A rag soaked with it should be laid upon the part, and when the burning is no longer endurable cosmoline applied. The power of oil of cloves in benumbing sensitive dentine or exposed nerve-pulp is well known. Altogether, the subject offers an inviting field for investigation.

AROMATIC BITTERS.

ANTHEMIS. U. S.—CHAMOMILE.

Roman or true Chamomile is the dried flowers of Anthemis nobilis, a composite of Europe. They are sometimes single, sometimes double. The single are more aromatic than the double florets. Chamomile contains a bluish or sometimes greenish volatile oil, a bitter principle, and a small amount of tannin. *Matricaria or German Chamomile* is the flowers of Matricaria Chamomilla, which are decidedly smaller than those of the ordinary chamomile, and have a stronger, less agreeable odor and taste. Their volatile oil is very similar to that of chamomile.

Therapeutics.—An excellent stimulant tonic; especially useful in convalescence. The dose of the *infusion* (*Infusum Anthemidis*—℥ss to Oj) is one to two wineglassfuls before meals.

Serpentaria. U. S.—*Virginia snake root* is the root of Aristolochia serpentaria and of A. reticulata, small herbal plants of the United States. It occurs as fine brittle rootlets attached to a small head, of a camphoraceous odor and taste, and contains a volatile oil, a yellowish-green resin, and a bitter principle. It is an elegant stimulant tonic, especially useful as an adjuvant to more powerful bitters. In overdose it is said to cause vomiting, and even purging. The dose of the *tincture* (*Tinctura Serpentariæ*—1 to 10, U. S.) is one to two fluidrachms; of the *fluid extract* (*Extractum Serpentariæ Fluidum*, U. S.), twenty drops.

Cascarilla, U. S., is the bark of Croton Eleuteria, a shrub growing in the West Indies. This bark occurs in quills or rolled pieces, and is to be distinguished by its outer grayish and inner deep-chocolate surface, by its spicy bitter taste, and the pleasant musk-like odor which it gives whilst burning. It contains tannin, volatile oil, and cascarillin, a neutral, bitter, crystallizable principle. Its therapeutic action is very similar to that of serpentaria. The dose of the *infusion* (*Infusum Cascarillæ*—℥i to Oj) is a wineglassful.

TRUE AROMATICS.

Cinnamomum. U. S.—*Cinnamon* is the bark of Cinnamomum Zeylanicum, a native of Ceylon, and of C. aromaticum, growing in China. The finest variety of cinnamon, that from Ceylon, occurs in long, closely-packed quills of a thin, very aromatic bark. *Cassia bark*, or *Chinese cinnamon*, is coarser, more broken, and less aromatic. Both varieties contain tannic acid and a yellowish volatile *oil* (*Oleum Cinnamomi*, U.S.), which on account of its great fragrance and very pleasant taste is largely used, in doses of from one to three drops, as an adjuvant, or to disguise the flavor of less agreeable drugs. *Cinnamon water* (*Aqua Cinnamomi*—fʒss to Oij, U.S.) is used solely as a vehicle. The *spirit of cinnamon* (*Spiritus Cinnamomi*—oil 1 to 10, U.S.) is administered in doses of half a fluidrachm; the *tincture* (*Tinctura Cinnamomi*—1 to 10, U.S.) in doses of one to two fluidrachms.

Pulvis Aromaticus. U.S.—*Aromatic Powder* (cinnamon, ginger, cardamom, nutmegs). An elegant carminative powder; dose, ten to twenty grains.

CARYOPHYLLUS. U.S.—*Cloves* are the unexpanded flowers of Caryophyllus aromaticus, a tree growing in the Molucca Islands. This aromatic, largely used as a spice, contains an exceedingly pungent volatile oil, officinal as *Oleum Caryophylli.* This is a yellowish oil, becoming dark by age, which, besides being used as a carminative and aromatic, is frequently employed to benumb sensitive dentine, or even exposed pulp, in *caries* of the teeth. Dropped on a piece of cotton and placed in the cavity, it will very frequently cure toothache. Dose, one to two drops. The *infusion*, or *clove tea* (*Infusum Caryophylli*—ʒii to Oj), is made with boiling water; the dose is a wineglassful.

MYRISTICA. U. S.—*Nutmeg* is the kernel of the fruit of Myristica moschata, a tree inhabiting the Molucca Islands. The nutmeg contains both a fixed and a volatile oil. Mace (*Macis*, U. S. P.) is the *arillus* or outer imperfect supernumerary coating of the seed. It contains a volatile oil identical with that of the nutmeg. The nutmeg is possessed of narcotic power, and it is said that one or two when taken will produce a dreamy, half-unconscious condition. I have found that injected into the jugular vein the volatile oil produces in the lower animals profound narcosis with abolition of all reflexes, and, finally, death from paralysis of the respiratory centres. The dose of the volatile oil (*Oleum Myristicæ*, U. S.) is from two to five drops.

PIMENTA. U. S.—*Pimento*, or *Allspice*, is the unripe berries of the Eugenia Pimenta, a tree, native of the West Indies. It contains a green fixed oil and a volatile *oil* (*Oleum Pimentæ*, U. S.), the dose of which is two to five drops.

CARDAMOMUM. U. S.—*Cardamoms* are the fruit of the Elettaria Cardamomum, which grows in the East Indies. They consist of tough, seemingly fibrous, generally more or less triangular capsules, containing a number of small, hard, very aromatic seeds. The capsule is itself dry and tasteless. In commerce cardamoms are divided into three varieties, according to their length. According to Trommsdorf, the seeds contain, besides 10.4 per cent. of fixed oil, 4.6 per cent. of a colorless, highly aromatic, volatile oil. Cardamom is a very grateful aromatic, much less stimulating and heating than most of the other substances of its class. The dose of the *tincture* (*Tinc-*

tura Cardamomi—1 to 6.6, U.S.) is half a fluidrachm. The *compound tincture* (*Tinctura Cardamomi Composita*, U.S.) is a very elegant addition to, or vehicle for, tonic medicines; dose, one to two fluidrachms.

ZINGIBER. U.S.—*Ginger* is the dried rhizome or root-stock of the Zingiber officinale, growing in the East and West Indies. *Green Ginger* is the *fresh* rhizome. The *Black Ginger* is the root-stock dried with the epidermis on; the *White* or *Jamaica Ginger* is the same, deprived of its epidermis. The fresher ginger is, the greater is its power, and by time and exposure it becomes completely inert. Its active principles are a soft, acrid, aromatic resin, and a yellow volatile oil. Ginger is much used in domestic medicine as a stimulant carminative in *colic;* given in hot water, it is also used as a sudorific and stimulant in the pain due to *suddenly-suppressed menstruation.* It is often added with advantage to other remedies in *dyspepsia.* The *syrup* (*Syrupus Zingiberis*, U.S.) is used only as a cordial drink or vehicle, in doses of from half a fluidounce to a fluidounce. The *tincture* (*Tinctura Zingiberis*—1 to 5, U.S.) is the most commonly employed; the dose is half a teaspoonful to a teaspoonful. The dose of the *fluid extract* (*Extractum Zingiberis Fluidum*, U.S.) is ten drops. The *oleoresin* (*Oleoresina Zingiberis*, U.S.) is employed as a stimulant addition to tonic pills; the dose is from half a minim to two minims.

PIPER. U.S.—*Black Pepper* is the unripe berries of the Piper nigrum, a woody vine-like plant growing in the East Indies. *White Pepper* is the ripe berries, stripped of their skin and dried. It is much inferior to the ordinary variety. The active principles of black pepper are a soft acrid resin, a pungent, fiery, volatile oil, and piperin.

In 1819 Oersted discovered *Piperin* (*Piperina*, U.S.), which crystallizes in colorless, glistening, four-sided, truncated prisms, of a neutral reaction, but capable of combining with acids to form salts. When pure it is tasteless; but very commonly it has a burning taste, due to the presence of some of the volatile oil of pepper. The possession of very active antiperiodic properties* has been claimed for piperin, and it was for a time employed in *intermittent* fever; but it has fallen into complete disuse. The dose as an antiperiodic is four grains repeated once or twice during the interval between the paroxysms. According to the observations of Prof. H. Kronecker and of Herr Fliess, piperin in the frog paralyzes the peripheral ends of the sensory nerves (*Archiv für Physiologie*, Leipzig, 1882, p. 111). In the rabbit its action upon the sensory nerves is much less marked. The respiratory and pulse rates are greatly accelerated, and death is finally caused by cardiac arrest (*Ibid.*, 1884). Pepper is very largely used as a condiment; but, as its taste is more hot than aromatic, it is rarely used internally in medicine, except as an addition to simple bitters or to antiperiodics, generally in the form of the officinal *oleoresin* (*Oleoresina Piperis*), the dose of which is a minim. In atonic *dyspepsia* the latter preparation is an excellent adjuvant to tonic pills. Dr. Schiffer is said (Fliess) to have used piperidin successfully in a case of vaginismus, by injecting 0.3 grain hypodermically near the vaginal entrance.

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* For a discussion of the subject, see *Die Pflanzenstoffe*, p. 492.

Capsicum. U. S.—The U. S. Pharmacopœia now recognizes only the small, less than an inch long, very fiery fruit of Capsicum fastigiatum, the *African Pepper*, or *Chillies*. The large, bright red, conical or ovate, comparatively mild peppers of the market are from C. annuum; they are sometimes known as *West India peppers.* Capsicum contains as its active principle an exceedingly acrid oleoresin. The name of *Capsicin* has been applied by different observers to the oil, to the resin, and to their combination, but should, I think, be dropped, as having no definite meaning.

Capsicum is a very powerful local irritant, its oleoresin when applied to the skin producing in a very few minutes intense pain and redness, and finally destroying the cuticle. In the alimentary canal it acts in a similar manner: thus, moderate doses produce merely a pleasant feeling of warmth in the stomach, whilst overdoses may cause gastro-intestinal inflammation, with severe pain as well as vomiting and purging. The chief use of *Cayenne Pepper* is as a condiment; yet it is often added with advantage to tonic pills to increase their immediate action on the stomach. When there is habitual feeble digestion, with flatulence, its free use on food may do good. In *adynamic disease*, especially as occurring among *drunkards*, capsicum is often very useful by stimulating the stomach up to the point of digesting food. *Locally*, either as the diluted tincture in a gargle, or applied in powder or tincture by means of a swab, it is useful in *severe tonsillitis*, especially in that accompanying scarlet fever.

Administration.—The dose of capsicum is four to five grains in pill form; of the officinal *Oleoresina Capsici*, which is to be preferred on account of its lesser bulk, from half a grain to one grain. The infusion (*Infusum Capsici*—℥ss to Oj) is used as a gargle. The *tincture* (*Tinctura Capsici* —1 to 20, U. S.) is employed locally, and is sometimes administered in half-fluidrachm doses to drunkards.

Oleum Cajuputi. U. S.—The *Oil of Cajeput* is obtained from the leaves of the Melaleuca Cajuputi, a tree growing in the Molucca Islands. This volatile oil is of a green color, peculiar fragrant odor, and burning, camphoraceous taste. It is not very irritating to the skin, and is exceedingly destructive to low forms of life, and consequently has been used as a *parasiticide* externally, and even internally against the Ascarides. I have never used it except as a carminative and aromatic stimulant in cases of *intestinal pain* and *spasm*, and in *serous diarrhœa.* When employed in these affections in combination with chloroform, camphor, and opium, it is very efficient. As a counter-irritant, it has been used in *rheumatism;* as a stimulant to the skin, in *psoriasis*, *acne rosacea*, and *pityriasis*. The dose internally is from ten to fifteen drops.

OLEUM SASSAFRAS. U.S.—The *Oil of Sassafras* is enormously used in the arts on account of its cheapness and pleasant flavor. It is capable of producing very marked narcotic poisoning (case, *Trans. Med. Chir. Faculty, Maryland*, 1884, 288), and is said to act upon the lower animals as a convulsant and narcotic.

AURANTII AMARI CORTEX—BITTER ORANGE PEEL, U. S.—The *fluid extract* (*Extractum Aurantii Amari Fluidum*, U. S.) and the *tincture* (*Tinctura Aurantii Amari*) may be given respectively in doses of twenty minims and a fluidrachm. AURANTII DULCIS CORTEX—SWEET ORANGE PEEL, U. S.—Of the *syrup* (*Syrupus Aurantii*, U. S.) the dose is a dessertspoonful, of the *tincture* (*Tinctura Aurantii Dulcis*, U. S.) a teaspoonful. The orange peels are themselves scarcely medicinal, but are officinal as affording preparations much used as vehicles. LIMONIS CORTEX, U. S., or *Lemon Peel* (*Spiritus Limonis*, U. S.), is also used for flavoring purposes.

AURANTII FLORES.—The flowers of the orange are officinal for the preparation of the *Orange Flower Water*—*Aqua Aurantii Florum*, U. S.—which is used as an elegant vehicle, free from medicinal properties.

The fruits of the following umbelliferous plants, Fœniculum vulgare, Carum Carui, Coriandrum sativum, Pimpinella Anisum, are officinal under the respective names of *Fœniculum* (*Fennel*), *Carum* (*Caraway*), *Coriandrum* (*Coriander*), *Anisum* (*Anise*). They all depend for their virtues upon volatile oils which are officinal. The Oil of Anise of commerce is chiefly the product of a Chinese tree, the Illicium Anisatum, or Star Anise, from whose five- to ten-rayed capsular fruit it is obtained by distillation. The *Aqua Fœniculi* and *Spiritus Anisi* are officinal. All of these fruits and their preparations may be used as carminatives and stomachics.

The herbal portions of the following mints are officinal: Lavandula vera, Rosmarinus officinalis, Salvia officinalis, Mentha piperita, Mentha viridis, Melissa officinalis. They are respectively known as *Lavender* (*Lavandula*), *Rosemary* (*Rosmarinus*), *Sage* (*Salvia*), *Peppermint* (*Mentha Piperita*), *Spearmint* (*Mentha Viridis*), and *Balm* (*Melissa*). The most important preparations of them are as follows: *Spiritus Lavandulæ Compositus*—*Compound Spirit of Lavender*, a very elegant and agreeable stomachic and cordial; dose, a fluidrachm to half a fluidounce. *Aqua Menthæ Piperitæ*—*Peppermint Water*, and *Aqua Menthæ Viridis*—*Spearmint Water*, both very frequently used as vehicles. *Spiritus Menthæ Viridis* and *Spiritus Menthæ Piperitæ*—*Essence of Spearmint* and *Essence of Peppermint*, used as carminatives, in doses of from ten to twenty drops. The *oils* of lavender,* rosemary, peppermint, and spearmint are also officinal, and may be used in doses of from three to ten drops as carminatives. Sage contains tannin.

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* MM. Masoin and Bruylant have studied to some extent the physiological action of the *oils of lavender, rosemary* (see, also, *Schmidt's Jahrbücher*, clxxx. 123), *marjoram*,

The volatile *Oil of Gaultheria* (*Oleum Gaultheriæ*, U. S.) is used for flavoring purposes. *Calamus*, the rhizome of the Acorus Calamus, also contains a volatile oil, and its infusion is sometimes used as a carminative.

EUCALYPTUS GLOBULUS. U. S.

The Eucalyptus globulus* is a large tree, native of Australia. The leaves, which are alone officinal, contain, besides tannic acid, a volatile oil, which, when pure, is nearly colorless, of a warm mint-like taste, with a bitter after-taste, and a very peculiar mint-like odor. It is freely soluble in ether, alcohol, and the fatty oils, and is obtained by distillation or by acting on the leaves

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and *aspic* (*Lavendula Spica* L.) (*Bull. Acad. Roy. Méd. Bruxelles*, 1879, 558). In frogs they cause generally paralysis with loss of reflex activity, the muscles being intact, and the sensory nervous apparatus affected before the motor. Upon the higher animals a similar effect was produced, except that oil of rosemary caused epileptiform convulsions. *Oil of Peppermint* (*M. Piperita*) has been studied by S. D. Markuson (*Inaug. Diss.*, Halle, 1877; *Schmidt's Jahrb.*, Bd. clxxx. 122), who finds that whilst very small doses increase, larger ones decrease the blood-pressure and lower the bodily temperature.

Menthol, or *Oil of Peppermint* (*Camphor*), has lately obtained great notoriety as a local anæsthetic, and, if freely rubbed upon a part, it undoubtedly will often relieve neuralgic pains when they are superficial and peripheral in their origin. Its physiological action has been studied by Paolo Pellacani (*Arch. f. Exp. Path. und Pharm.*, xvii. 376). In the frog it causes paralysis, first of the spinal centres and finally of the nerve-trunks. In the mammals both mobility and sensibility are depressed, the animal grows cold, the respiration becomes slow and shallow. Small doses excite, larger paralyze the frog's heart. In the poisoned mammal there were very curious, unexplained, rhythms of rise and fall of the blood-pressure.

* Attention was first called by Labillardière to the value of the Eucalyptus globulus in 1792, but it was not until 1860 that M. Ramel commenced the culture of the tree in Paris and induced the Prefect of the Seine to order its cultivation on a large scale. Since that time it has been largely introduced into Europe, Algeria, South Africa, and California, and in some of these countries planted forests are now growing and spreading. The tree is remarkable for combining extreme hardness of wood with a rapidity of growth asserted to be about five times that of our ordinary trees; it is even affirmed that shingles made of it are fire-proof. Its capability for absorbing and evaporating water is also extraordinary, and to it has been attributed the freedom of Australia from malarial climatic influences. Indeed, it is stated that a tree will evaporate ten times its weight of water in twenty-four hours, and numerous examples are given in which swamps in Europe and Algeria have been rapidly converted by it into dry ground. It is believed to destroy malaria not only by draining the soil, but also by yielding balsamic exudations to the air. however this may be, there is at present very strong evidence as to its power of rendering infected districts healthy. As, however, the consideration of this belongs to the subject of hygiene rather than of therapeutics, the reader is referred for detailed information to the following memoirs: Regulus Carlotti, *L'Eucalyptus, son Rang parmi les Agents de la Matière Médicale*, Ajaccio, 1872; M. Gimbert, *L'Eucalyptus Globulus, son Importance en Agriculture, en Hygiène et en Médecine*, Paris, 1870; Waterer, *Bulletin de la Société d'Acclimatation*, 1872; *London Medical Record*, Dec. 1873; *London Lancet*, ii., 1877.

Under the name of Eucalypsinthe, a liquor distilled from its leaves has appeared in European commerce.

with ether. It does not undergo oxidation into a resinous mass on exposure to the air, and is remarkable for its power of resisting the influence of concentrated sulphuric acid. It has been affirmed that the leaves of Eucalyptus contain also an alkaloid; but Rabuteau (*Bulletin Thérap.*, lxxxiii. 549) has fairly demonstrated that this is an error. All the virtues of the remedy probably reside in the volatile oil, which is in greatest abundance in the leaves. According to the researches of Stanislas Martin (*Bulletin Thérap.*, lxxxiii. 453), the oil is entirely absent from the bark of plants grown in Southern France and Corsica, but exists in that from Australia and Algeria.

PHYSIOLOGICAL ACTION.—Locally, the oil of Eucalyptus acts as a decided but not very intense irritant, and the first effect of large doses is burning in the mouth and fauces, with increased secretion of saliva, followed very soon by a feeling of warmth in the stomach.

The general effect of the same dose of the oil appears to vary considerably in different individuals; but the following summary comprises the facts as nearly as may be. After the ingestion of from ten to twenty drops, a period of mental and physical activity is often apparent, followed by a feeling of calm and serenity. By somewhat larger doses, or in susceptible persons by the doses mentioned, increased disturbance of the digestive organs, ending often in loose stools having the odor of the oil, with augmentation in the frequency and force of the pulse, is produced. Gubler adds to these symptoms increase of temperature; but in Gimbert's experience febrile manifestations, although occasionally occurring, were not usually present. In some cases the medicine acts very disagreeably, producing violent cardiac palpitations or intense headache: how far these are directly dependent upon the drug, or are sympathetic upon its local action on the stomach, is uncertain. If the dose be repeated, or if a larger amount be taken at once, a period of sedation manifests itself; the pulse loses its force, and the animal temperature is abated. After doses of seventy-five grains, Binz noted numbness of the limbs, with a feeling of excessive weight in them. If the use of the remedy be persisted in, a state of asthenia is induced; the temperature falls as much as a degree and a half, and the pulse even to fifty (Gimbert, *Archives Générales*, 1873, xxi. 141); the respiration becomes less frequent; the muscular weakness is extreme, so that raising the arm to the mouth is painful; the sensations are blunted, but the intellect is absolutely unaffected. In an old man who took eighty drops, the power of motion almost disappeared, and he affirmed that he lost for the time being all sense of the presence of his limbs, so that he was unconscious of possessing them when he shut his eyes, although his intellect was perfectly clear throughout.

Upon the lower mammalia the oil of Eucalyptus appears to act precisely as it does on man. According to the experiments of Gimbert, the hypodermic injection of the oil is immediately followed by a period of excitement, seemingly in great measure due to the intense local irritation; after about half an hour, if the dose has been sufficiently large, the animal begins to stumble and totter in walking, the breathing grows more and more slow and irregular, the limbs give way, the ears droop, the muscular weakness becomes profound, and death, preceded often by partial convulsions, occurs through failure of respiration. In Gimbert's experiments the heart always continued to beat after breathing had ceased. As the motor nerves and the muscles retained their functional power after death, the failure of motility and reflex activity must have been central, and Gimbert concludes that the drug in toxic doses is therefore a paralyzant to the spinal cord and the medulla. This conclusion was also attained experimentally by Binz (*British Medical Journal*, i., 1874). Various observers accord in stating that, after toxic doses, there is, in animals, a decided fall of temperature. It would appear from the experiments of Hermann Schläger that, after hypodermic injections, the temperature sometimes rises, probably as the result of the local irritation (*Die Physiol. Wirk. Eucal. glob.*, Inaug. Diss., Göttingen, 1874). The same observer noted that the arterial pressure was greatly lessened. As this fall occurred after paralysis of the parvagum, by section or by atropia, and also after vaso-motor paralysis by section of the cord, it must be due to a direct action upon the heart. This was confirmed by the direct influence of the drug upon the cut out heart of the frog. The oil is probably eliminated by the lungs, skin, and kidneys. In the experiments of Prof. Binz, the day after the ingestion of seventy-five drops, the breath smelt of the drug, and the perspiration of amylic alcohol. The urine began to have the odor of the oil an hour and a half after its ingestion, and continued to have it for thirty-six hours. Dr. Gimbert states that the odor imparted to the urine resembles that of violets, and is very similar to that caused by turpentine.

Binz states that upon the lower infusoria the oil acts even more powerfully than does quinia, and its antiseptic properties are without doubt very great (Gimbert, *Archives Générales*, xxi. 137). Mosler (*Deutsches Archiv für Klin. Med.*, 1872, x. 160) affirms that in dogs whose spleens were exposed, injections of tincture of the leaves of the Eucalyptus produced a decided contraction of the viscus. According to Gimbert, the excretion of urea is enormously increased by the use of the drug.

THERAPEUTICS.—The chief use that has been made of Eucalyptus is as an antiperiodic. So far as I know, Dr. Joseph Keller (*Wiener Medizinische Wochenschrift*, xxii., 1872) has employed it upon a larger scale than any one else. He used it in four hundred and thirty-two cases, of which two hundred and ninety-three had suffered from previous attacks. Of the tertians 75.57 per cent., of the quartans 70 per cent., and of the quotidians 67.89 per cent. yielded to the remedy. He recommends it as especially valuable in obstinate cases in which quinine has been taken again and again. Lorinser (*Wiener Medizin. Wochenschrift*, xix., xx.), Haller (*Wiener Medizin. Wochenblatt*, xxvi.), Bohn (*Berlin. Klin. Wochenschrift*, 1872), Carlotti (*loc. cit.*), Cortan (*Montpellier Médical*, May, 1872), Gimbert (*loc. cit.*), Gubler (*loc. cit.*), Tristany, of Spain (*Buchner's Repertorium*, xix., 1870), and others, bear more or less urgent testimony to the value of Eucalyptus in malarial diseases; whilst Brudell (*Bulletin Thérapeutique*, May, 1875), Seitz (*Bayer. ärztl. Intell. Blatt*, 1870), and Papillon (*Gazette Hebdomadaire*, 1872) affirm it to be of comparatively little or no value. The weight of testimony is vastly in favor of the possession of decided antiperiodic powers by Eucalyptus; but it is exceedingly improbable that it will ever supersede the cinchona alkaloids: where these have failed, or for any reason cannot be taken, it may be used with good hope of success.

Gimbert, Gubler, and Carlotti all claim excellent results from the use of Eucalyptus in *bronchitis*, both acute and chronic: in the first variety it is not to be given until the acuteness of the symptoms has been relieved and free expectoration established, which, as a rule, is about the end of the second week. The remedy is also asserted to be of value in *asthma*, and even in *catarrhal phthisis*. As the oil is eliminated by the kidneys, it comes into contact with the urino-genital mucous tract, and has been employed in affections of the same; it seems to be less active than copaiba, and the results obtained in *gonorrhœa* by Aron (*Schmidt's Jahrbücher*, Bd. clvii., p. 239) were not very good. The remedy appears to be safer than copaiba in the early stages of the disorder. The drug has also been employed in *hemorrhages*, in *intestinal catarrh*, in *nasal catarrh*, and similar disorders; it seems to act somewhat similarly to turpentine in these cases, but to be less stimulating. It appears well established that Eucalyptus possesses decided antiseptic powers: dry dressings of gauze, lint, etc., impregnated with the oil may be used; or, as in Australia, the bruised leaves may be applied to the wound. (For *résumé* of evidence and method, consult *Australasian Med. Gazette*, iii. p. 72; see, also, *Berl. Klin. Wochens.*, xix. 524.)

ADMINISTRATION.—The oil (*Oleum Eucalypti*, U. S.) offers the most eligible preparation of Eucalyptus: in *bronchitis* from four to ten drops of it may be given in emulsion or capsules at intervals of two or three hours, as an antiperiodic, from half a drachm to a drachm may be exhibited two or three hours before the expected paroxysm. The saturated *tincture* made from Australian or Algerian leaves is efficient; dose, a drachm to half an ounce. The dose of the *fluid extract* (*Extractum Eucalypti Fluidum*, U. S.) is one to two fluidrachms.

MINERAL TONICS.

FERRUM—IRON.

Since iron constitutes a necessary integrant portion of the red blood-corpuscles, it is a food rather than a medicine. A very large proportion of the various articles of ordinary diet contain a trace of it; and as, according to Quevenne, it is very rarely to be found in normal urine, it must accumulate in the system. When, however, the supply, from any cause, is insufficient, or the power of digesting and assimilating it is impaired, or an abnormal excretion of it occurs, or by direct discharge it is drawn off from the blood, as in hemorrhage, a less than normal amount of it exists in the body. When this is the case, the condition ordinarily known as *anæmia* existing, the circulating fluid contains comparatively few red disks. It is this state which constitutes the great indication for iron. Under its use, if the cause of the anæmia be prevented from operating continuously, the color returns to the cheeks, because there is an absolute increase of the hæmato-globulin in the blood. Thus, Prof. Simon (*Animal Chemistry*, London, 1845, Syd. Soc. ed.) reports a case of chlorosis in which, under the steady use of iron for sixty-four days, the globulin increased from 30.86 parts to 90.80 parts per thousand, and the hæmatin from 1.431 parts to 4.598 parts per thousand; and Cutler and Bradford (*Amer. Journ. Med. Sci.*, 1878, p. 78) have obtained confirmatory results with Malassez's tubes. This increase is certainly due in part simply to the supply of the peculiar food of the red corpuscles; but it seems probable that the iron acts not merely as a food, but also as a veritable stimulant to the organs which produce these bodies. Since, however, we have no definite knowledge as to the early history of the red disks, it is evident that any theory as to the method in which iron increases their number must be a mere conjecture. It has been generally believed that iron, given to the healthy subject, would induce a condition of excess of the red blood-corpuscles. Recent exact investigations, whilst somewhat in discord, offer evidence calculated to unsettle our belief. The experiments of Nasse (*Lond. Med. Record*, 1877, p. 498) upon dogs are in favor of the older view, whilst those of E. C. Cutler and E. H. Bradford are in opposition to it.* The first observer giving iron with fat, noted not only an increase of bodily weight, but that the specific gravity of the blood rose from 1052 to 1060.8, and the amount of the metal in the blood from 0.477 to 0.755 per thousand parts, both the result of increase in the corpuscular element. Cutler and Bradford experimented upon man, using the tubes of M. Malassez, the result being slight diminution of the red blood-disks. As, however, the experiments were only two in number, and the subjects not under complete control as to conditions of life, their observations can hardly be considered conclusive.

It appears to be a well-established fact that one of the functions of the red blood-corpuscles is to convert oxygen into ozone, which is the efficient form of the element in the system (see paper by A. Sasse, *Vierteljahresschrift für Prakt. Heilkunde*, 1866, zweiter Band). The oxide of iron outside of the body certainly possesses an ozonizing power similar to that of the red disk.

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* Drs. V. H. Meyers and F. Williams (*Arch. Exper. Path. u. Pharm.*, xiii. 76) have studied the effects of enormous doses of the tartrate of iron and sodium upon the lower animals. Both frogs and mammals are killed by it: the symptoms in warm-blooded animals being vomiting, purging, great fall of the blood-pressure, muscular weakness, finally coma and death. The experiments show that the heart is not much affected, but the vasomotor system and the spinal-motor centres are paralyzed.

Thus, a spot of iron mould, *i.e.*, iron oxide, on linen will in time destroy the fabric. The reason of this is the corroding action of the ozone which is slowly generated by the oxide of iron. From a similar cause a fleck of rust on a bright surface of steel will steadily enlarge and deepen. It would seem *a priori* probable that in the blood iron acts as it does out of the body. If this be so, by increasing oxidation an increase of the iron in the blood should cause elevation of temperature and increased elimination of urea. The studies of W. Pokrowsky (*Virchow's Archiv*, Bd. xxii.) have shown that, in cases of anæmia, after the exhibition of iron the temperature does rise, even when in the beginning it was not below normal, and that simultaneously there is an increase in the daily elimination of urea; and the experiments of Botkin, as quoted by Sasse (I have not seen the original), establish the same fact in regard to healthy men. The increased oxidation cannot be due simply to an increase in the number of the red corpuscles, for whilst the latter accrues slowly, Pokrowsky found that the temperature sometimes rose within five hours after the exhibition of the first dose. It would seem, therefore, that iron acts directly on the blood as an ozonizing agent.

Iron in very minute quantity (Quevenne, *Mémoire sur l'Action physiologique et thérapeutique des Ferrugineux*, *Arch. de Physiol., de Thérapeutique et d'Hygiène*, Oct. 1854, p. 93) is at times present in normal urine, and the exhibition of it as a medicine increases the percentage. According to the researches of Quevenne (p. 95), the elimination of the ordinary medicinal salts of iron is always very slight; but the experiments of Becquerel (*Simon's Chemistry*, vol. ii. p. 264) are not in accord with this. The amount of iron in the urine was found by him to vary, in those taking ferruginous preparations, very greatly and unaccountably from day to day, but the elimination commenced as soon as the administration. According to Quevenne, the haloid salts escape in the urine much more freely than do the other preparations.

Almost all of the preparations of iron are more or less astringent, and when in the blood very probably exert a direct influence upon the tissues, contracting them not merely by increasing their tone, but also by acting on their vital contractility.

The preparations of iron may be divided into those which are soluble and those which are insoluble in water. At first sight it would appear that the former class of preparations would be those most readily absorbed. The experiments of Quevenne (*loc. cit.*) have, however, demonstrated that these soluble preparations are largely precipitated by the gastric juice even when it is strongly acid. This precipitate is probably an albuminate, mixed, when the gastric juice is alkaline, with the oxide of the metal. It has been further demonstrated by Quevenne that these precipitates do not yield so large a percentage of material to the acid gastric juice as do some of the insoluble salts. According to Mialhe (*Chimie appliquée*, Paris, 1856), after the entrance of an iron salt into the blood its power of acting as a ferruginous tonic depends upon its capability of being decomposed by the alkalies of the blood in such a way as to give origin to albuminates. From these considerations it would appear that the question of solubility in water is of very little importance in the choice of a chalybeate. Quevenne has demonstrated that the reduced iron yields the largest percentage, and, as it is nearly free from astringency, it is probably the best chalybeate. If a soluble preparation be desired, the ammonic or potassic tartrates are very unirritating. If Mitscherlich be correct in his deductions, the protosalts are more readily absorbed than the sesquisalts, and consequently should be preferred as a general rule.*

There are some persons in whom iron produces headache; this can only sometimes be obviated by the use of laxatives. The observations of M. Petit, Dr. N. A. Bubnow, etc. (*Zeitsch. f. Physiolog. Chem.*, vii.), that the iron preparations in large doses inhibit the digestive processes, throw some light upon these cases.

When iron is exhibited in the usual doses, but a small proportion is absorbed, the remainder escaping with the fæces, to which it imparts a black color. This black color is due to a conversion of the iron into tannates and sulphurets; the tannic acid of the first compound being derived from the food, the sulphur of the second from the intestinal gases.

THERAPEUTICS.—The chief indication for the use of iron is the existence of *anæmia;* the contra-indication, a state of *plethora:* on these points sufficient has already been said, and the peculiar actions of certain salts will be considered under their respective preparations. The preparations of iron which are recognized by the U. S. Pharmacopœia are unnecessarily numerous.

FERRUM REDUCTUM—REDUCED IRON. U.S.—This preparation is also known by the names of *Ferri Pulvis*, *Iron by Hydrogen*, and *Quevenne's Iron*, and is as a chalybeate the best of all the various medicinal forms of iron. It is made from the subcarbonate (sesquioxide) by exposing it at a white heat to the action of hydrogen, which takes away the oxygen and leaves the pure metallic iron. It occurs as a light, iron-gray, tasteless powder, which should be completely dissolved by dilute sulphuric acid without yielding the odor of sulphuretted hydrogen, and when touched with a lighted taper should ignite and burn to the brown oxide of iron. If it be black, or if it fail to answer the tests given above, it is impure, and indeed, as offered in the shops, not rarely it is entirely spurious. Of all the efficient preparations of iron it is the freest from astringency. The dose is from two to five grains, taken in pill form after meals. As it is entirely tasteless, it is frequently given to children in chocolate-drops or lozenges, which are taken as confectionery.

FERRI OXIDUM HYDRATUM—HYDRATED OXIDE OF IRON. U. S.—The *Hydrated Sesquioxide of Iron*, made by precipitating the tersulphate with ammonia, is a reddish-brown powder, which is used solely as an antidote to arsenic. For this purpose it should be freshly prepared, and should be so moist as to constitute a magma. Its virtues are deteriorated by age, even when it is kept under water, and are entirely destroyed by drying. If the solution of the tersulphate of iron be not at hand in an emergency, the perchloride will yield just as useful a product, and carbonate of sodium may be substituted, if circumstances necessitate it, for the ammonia. The precipitate falls at once, and may be washed by putting it in a piece of muslin, squeezing out the original fluid, and then pouring on some fresh water. As the sesquioxide of iron is perfectly innocuous, it should be very freely administered when used as an antidote, especially since it only acts when in excess. A teaspoonful to a tablespoonful of it should be stirred up in water and taken at once, the dose being repeated several times if necessary. The *Ferri Oxidum Hydratum cum Magnesia*, U.S., differs from the hydrated oxide in containing magnesia, which is substituted in excess for the ammonia as a precipitant. As magnesia is not at all irritant, and is itself antidotal to arsenic, this new preparation offers decided advantages over the older antidote. It should be given promptly and freely.

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* I have left this as in earlier editions, although it seems to me that the subject of the absorption of iron urgently needs re-investigation; see also *Berlin. Klin. Wochensch.*, 1877, p. 420.

FERRI CARBONAS SACCHARATUS. U.S.—SACCHARATED CARBONATE OF IRON.—This greenish-gray powder is made by precipitating a syrupy solution of the sulphate of iron by bicarbonate of sodium. Throughout the subsequent washings, and during drying, sugar is kept constantly present in large amount, so as to prevent the absorption of oxygen, and the consequent conversion of the protocarbonate into the sesquioxide. This is a very good chalybeate, nearly free from astringency, and may be given in doses of from three to five grains, in pill form. *Pilulæ Ferri Compositæ*, U.S., contain the protocarbonate of iron and myrrh. They are sometimes used in anæmia with amenorrhœa; one to three pills three times a day. The *Mistura Ferri Composita*, U.S., is a liquid preparation containing substantially the same ingredients as the compound pills. Dose, one to two tablespoonfuls.

FERRI SULPHAS—SULPHATE OF IRON. U.S. ($FeO,SO_3 + 7HO - FeSO_4 + 7H_2O.$). The pure protosulphate of iron is made by dissolving iron in dilute sulphuric acid. It occurs in transparent efflorescent rhombic prisms of a pale bluish-green color and a metallic styptic taste. The sulphate of iron is a very decided astringent, and in a concentrated form and sufficient amount acts as an irritant poison, producing vomiting, purging, and gastro-intestinal inflammation.* Externally its solution (five to twenty-five grains to the fluidounce) is used as an astringent lotion. It has been especially recommended in this form (℥i to Oj) in *erysipelas*. As a simple chalybeate the sulphate of iron should never be used. In *chronic diarrhœa* it is sometimes employed as a tonic astringent. Dose, five grains; in the form of the dried sulphate (*Ferri Sulphas Exsiccatus*, U. S.), three grains. *Ferri Sulphas Præcipitatus*, U. S., is simply a pure ferrous sulphate obtained by precipitation, and may be used instead of the older preparation.

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* In a case reported in *New York Med. Journ.*, xxxviii. 401, the early symptoms, as stated by the patient, were chiefly nervous; little confidence can, however, be reposed in the patient's report of symptoms or of the amount ingested.

LIQUOR FERRI SUBSULPHATIS—MONSEL'S SOLUTION. U.S.—The *solution of the subsulphate* [of the sesquioxide] *of iron* (often incorrectly called solution of the persulphate of iron) is a most powerful astringent and styptic, and is used solely as such. It is but slightly irritant, and is the best of all the astringents for staunching hemorrhage when it can be applied directly to the part, as in external wounds, or in *hæmatemesis*. In hemorrhage from the stomach, ten drops of it may be given in a tablespoonful of water, the dose being repeated as necessary. Applied by means of the atomizer, it is often very efficient in *hæmoptysis*. In such a case the fluid to be atomized should have the strength of from five to twenty drops to the ounce. The inhalation should last from five to fifteen minutes, and be repeated at intervals of an hour or longer. It is very essential that the liquid should be finely pulverized. In *diphtheria*, Monsel's solution is very valuable applied freely, of full strength or diluted *pro re nata*, to the throat every three to twelve hours.

The *Solution of the Tersulphate* (LIQUOR FERRI TERSULPHATIS, U.S.), owing to its irritant action, is used only to make the sesquioxide preparations.

TINCTURA FERRI CHLORIDI—TINCTURE OF CHLORIDE OF IRON, U.S., contains the sesquichloride of iron, muriatic acid, and alcohol, and, from the reactions of the last two ingredients, muriatic ether. It is prepared by adding alcohol to the officinal *Liquor Ferri Chloridi*, and is a reddish-yellow, astringent, irritating, somewhat corrosive liquid. It is an excellent chalybeate, possessed of peculiar properties, probably in some measure due to the ether which it contains. It is a diuretic, increasing often very decidedly the daily urinary secretion. It appears also to exert an astringent influence upon the urino-genital mucous membrane, and is frequently employed with tincture of cantharides in *gleet*. In *chronic Bright's disease* it is often of very great service as a chalybeate diuretic. In *erysipelas* it is constantly employed with remarkable results, controlling the disease in a manner not yet understood. Analogy has suggested its employment in other adynamic affections, such as *diphtheria* and *pyæmia*, but its value in these diseases is much more doubtful. Locally it is used as an astringent in sore throat; for this purpose its strength should be reduced at least one-half. As it is very destructive to the teeth, care ought to be exercised in its use about the mouth, and also in its administration. The dose is from fifteen to thirty drops, given as a chalybeate three times a day; in erysipelas, every two or three hours. The orange-yellow crystalline deliquescent *Sesquichloride of Iron* (FERRI CHLORIDUM) (Fe_2Cl_3 — Fe_2Cl_6) is officinal, but is very rarely used.

SYRUPUS FERRI IODIDI. U.S.—The *Syrup of Iodide of Iron* contains 7.33 per cent. of the dry protiodide of iron in the fluidrachm, and is made by shaking iron, iodine, and water together, and adding hot syrup. It is a transparent, greenish liquid, of a sweet, ferruginous taste. It deposits no sediment on keeping, and should not affect the color of starch. If it strikes a blue color with the latter substance, it contains free iodine. The syrup of iodide of iron is a favorite remedy in those cases of anæmia in which there is a distinct scrofulous taint. It is believed to possess the peculiar alterative powers of iodine, conjoined with the tonic properties of iron. It is enormously used in *scrofulosis* occurring in anæmic children; but it certainly possesses no advantages over a ferruginous tonic and iodine when given separately but simultaneously Indeed, it seems to me uncertain whether its use is as effective as the separate administration of iodine and iron. The dose of it for a child two years old is five to ten drops; for an adult, thirty to forty minims. As it affects the teeth very seriously, it should always be freely diluted when taken, and the mouth should be well washed after its administration.

FERRI IODIDUM SACCHARATUM. U. S.—*Saccharated Iodide of Iron* is a yellowish-white or grayish powder which represents the chemical and medical properties of the corresponding syrup, being prepared by a parallel process. It may be substituted for the syrup in doses of from two to five grains given in pill form.

DIALYZED IRON.—*Ferrum Dialysatum.*—This is a clear, neutral, nearly tasteless, dark-red liquid, prepared by dialyzing a solution of the chloride of iron. Its exact chemical composition is uncertain. It contains a minute proportion of chloride, and it is possible that the iron exists as a basic oxychloride. It bears dilution with pure water, but is at once precipitated by alkalies, almost all soluble salts, and many organic substances. As the iron oxide in this condition is unable to pass through animal membranes, it has been asserted that it cannot be absorbed. Clinical experience shows, however, that it is absorbed, and it, *a priori*, seems certain that the dialyzed iron must undergo change the moment it enters the stomach. In what form absorption takes place we do not know. The tastelessness, harmlessness to the teeth, comparative freedom from astringency, have rendered it a favorite chalybeate, notwithstanding its feebleness; the assertion frequently made that it never constipates is an error. It should never be used in combination. The dose is twenty to forty drops. Dialyzed iron seems to be the best antidote at command for arsenic. It is harmless, and in cases of poisoning a tablespoonful should be administered at once, and repeated *pro re nata* (see *Philad. Med. Times*, vol. viii. pp. 104, 151, 335).

There are four officinal *Citrates of Iron*, all soluble in water.* Two of these

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* Dr. Glaevecke has (*Arch. Exper. Path. u. Pharm.*, xvii. 466) experimented upon rabbits by the hypodermic injection of citrate of iron. He finds that the iron appears in

(FERRI CITRAS and FERRI ET AMMONII CITRAS) occur in garnety-red scales, and are simply mild chalybeates. Dose, five grains. The *Citrate of Iron and Quinia* (FERRI ET QUININÆ CITRAS) is in transparent scales, varying from reddish brown to yellowish brown in color, with a tint of green. The *Citrate of Iron and Strychnia* (FERRI ET STRYCHNINÆ CITRAS) contains one per cent. of strychnia.

There are two officinal *Tartrates of Iron* (FERRI ET AMMONII TARTRAS and FERRI ET POTASSII TARTRAS), both occurring in garnety scales, and soluble in water. Dose, five grains. The *Lactate of Iron* (FERRI LACTAS, U. S.) occurs in greenish-white crystalline crusts or grains, soluble in forty-eight parts of water. It is a good chalybeate. Dose, five grains. There are two officinal *Phosphates of Iron*, which may be used in five-grain doses. FERRI PHOSPHAS is a bright slate-colored insoluble powder. FERRI PYROPHOSPHAS is an excellent preparation, occurring in apple-green scales, somewhat soluble in water, and nearly free from astringency and ferruginous taste. The *Ammonio-ferric Alum* (FERRI ET AMMONII SULPHAS, U. S.) occurs in octahedral crystals, of a pale violet color. It is freely soluble in water, is very astringent, and is only used in atonic *leucorrhœa*, in which affection marked benefit is often gained by the exhibition of it in five-grain doses three times a day. The *Bromide of Iron* (not officinal) has recently been highly recommended by Dr. Da Costa in chorea and incontinence of urine in children (*Medical and Surgical Reporter*, 1874). He gives, to a child, five grains, dissolved in syrup, and rapidly increases the dose to twenty grains. In a few trials, I have found it useless in chorea.

MANGANESE.—The *Black Oxide of Manganese* (MANGANI OXIDUM NIGRUM, U. S.), and the *Sulphate* (MANGANI SULPHAS, U. S.), have been supposed by some to possess therapeutic properties similar to those of iron. The metal manganesium certainly exists in the blood, but its salts have failed to gain the confidence of the profession, although highly recommended by Harmon, of Belgium, and by Pétrequin (*Nouvelles Recherches du Manganèse*, 2d ed., Paris, 1852, also *Bulletin Thérapeutique*, March, 1852) as an adjuvant to the chalybeates. In Dr. Garrod's experiments upon anæmia (*Medical Times and Gazette*, 1863) the preparations of manganese failed to be of service. C. C. Gmelin is said (*U. S. Dispensatory*) to have found the sulphate act as a powerful cholagogue on the lower animals; and Dr. Thomson states that it is a purgative to man in doses of one or two drachms. Dr. Leand affirms (*Glasgow Medical Journal*, Jan. 1865) that the oxide of manganese is therapeutically equivalent to the preparations of bismuth excepting in

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the urine in half an hour; that the maximum proportion is reached in two to four hours, and that after twenty-five hours elimination ceases. In man he states that these injections are well borne, and the therapeutic effects satisfactory; the dose of the citrate used for an adult was about 1.5 grains.

that it does not constipate, and that it may be used with advantage in *gastralgia*, *pyrosis*, and similar stomachic derangements.

ACIDUM SULPHURICUM—SULPHURIC ACID. U.S.

Oil of Vitriol ($SO_3,HO — H_2SO_4$) is when pure a colorless, heavy liquid (sp. gr. 1.843). On exposure to the air it rapidly absorbs moisture and becomes less dense. When its specific gravity is 1.78, it deposits crystals of the bihydrated acid at 28° F., and may burst the glass in which it is kept. Owing to its great affinity for water, it is used in chemistry as a desiccant.

Physiological Action.—Concentrated sulphuric acid is powerfully corrosive of both animal and vegetable tissues, abstracting the elements of water and leaving the carbon untouched. It consequently *blackens* organic matter at the same time that it destroys its texture.[*] When administered in therapeutic doses and absorbed into the blood, it is converted into sulphates, and as such, so far as is known, is eliminated.

It escapes by the kidneys, as has been proven by Dr. H. Bence Jones (*Lectures on Pathology and Therapeutics*, London, 1867) in regard to large therapeutic doses, and is attested by Maukopff as occurring after poisoning. As, however, the amount of elimination by the kidneys seems to be slight, it is very probable, as Dr. Headland (*Action of Medicines*, London, 1852) conjectures, that it is excreted both by the lower bowel and by the skin. Locally applied, dilute sulphuric acid is an astringent, and clinical experience proves that it exerts a similar action when taken into the system. Under such circumstances its astringent influence is most marked upon the skin and intestine,—parts which are believed to excrete it: it is therefore possible that this action is in a measure local, and dependent upon the presence of the excreted acid.[†]

Therapeutics.—Concentrated sulphuric acid is not rarely used as an escharotic, for which purpose it is mixed with finely-powdered charcoal so as to form a paste. Appropriately diluted, it has been used as a stimulant and astringent lotion in *venereal* and other indolent *ulcers*. Internally, sulphuric acid is very useful as an astringent in *colliquative sweats* (*night-sweats*) and in profuse *serous diarrhœas*. I have used it with great advantage in the sudden serous vomiting and purging of infants known as *cholera infantum*.

It has been employed with advantage in *cholera*, and a remarkable series of observations by Dr. R. G. Curtin (*Philadelphia Medical Times*, vol. iii. p. 649) at least furnish good reason for further testing its powers as a prophylactic against this disease. The facts recorded by Dr. Curtin are as follows. A very severe epidemic of the disease ceased in the Insane Department of the Philadelphia Almshouse within twelve hours after the lunatics were all put upon the free use of sulphuric acid lemonade; the only new case after this being in a man who refused to use the prophylactic. Two days after the use of the sulphuric acid was stopped, two new cases occurred, and the epidemic was again arrested by the use of the acid. In the surgical wards of the Hospital Department the acid was used from the beginning of the epidemic; and these wards, although in no way isolated, were the only parts of the institution unvisited by the disease.

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[*] The observation of Oro (*Comptes-Rendus*, 1875), that considerable quantities of dilute acids can be injected into the blood without causing coagulation or serious disturbance, has been confirmed by Dr. Paul Guttman (*Virchow's Archiv*, Bd. lxix. p. 534). The acid is probably at once neutralized by the alkali of the blood.

[†] The action of large but not corrosive doses of mineral acids upon animals has been to some extent studied by Dr. F. Hofmeister (*Prager. Med. Wochensch.*, 1879, iv. 75). Death, he believes, results from asphyxia, due to the acidification in the blood of the alkaline salts, which serve as vehicles in carrying the carbonic acid from the tissues.

Sulphuric acid was formerly used in *hemorrhages*, but is now rarely employed. It is, I think, much less efficacious than some other remedies. In *acute lead-poisoning* the dilute acid is an efficient antidote, and it has been proposed by M. Gendrin (Dr. Bennett, *London Lancet*, 1856) as a remedy in *chronic lead-poisoning*. As, however, he combined its internal exhibition with the daily use of warm sulphur-baths, it is doubtful how much of the successful result was due to its action. It is difficult to perceive how it can do good in these cases, and I do not think the clinical proof that it does so has as yet been brought forward.

TOXICOLOGY.—When swallowed in concentrated form, sulphuric acid acts as a corrosive poison. Death from collapse has resulted in two hours and a half (case in *Medical Times and Gazette*, vol. i., 1863), but usually the course of sulphuric acid poisoning is much more protracted, the fatal result having been delayed in some cases for several months. The usual symptoms are pain in the mouth, throat, and epigastrium, violent vomiting, often of tarry matters, with symptoms of collapse, such as cold extremities, feeble pulse, suppressed voice, and clammy skin. The mind is generally clear to the last. Profuse, and sometimes bloody, salivation is commonly present. The parotids sometimes swell as early as the fourth day, and Maukopff (*Syd. Soc. Year-Book*, 1863) has seen suppurative parotitis apparently induced by closure of the duct of Steno, retention of secretion, and consequent irritation of the gland. The later symptoms are those of ulceration of the œsophagus and stomach, and need not be dwelt upon here. The larynx is often profoundly affected. There is a very marked increase in the amount of sulphates in the urine, which may be albuminous and contain granular casts. Desquamative nephritis may be developed several days after the subsidence of the first symptoms. Thus, in one of the cases reported by Maukopff, urine which had ceased to be albuminous on the third day became so again on the twentieth, with a simultaneous development of casts containing blood-corpuscles; after death tubular nephritis was found. Another symptom noted by Maukopff was intercostal neuralgia.

After death, greater or less destruction of the œsophagus and stomach, or of the air-passages, is found. The black color of the slough is a diagnostic sign which an examination of the mouth will sometimes render available before death.

The most important part of the treatment of sulphuric acid poisoning consists in the immediate and free exhibition of the antidotes, which should be given in milk or in water. The best antidotes are chalk, magnesia, whitewash, and soap. Christison condemns the use of the alkaline carbonates, because they are themselves irritating. As, however, in these cases time is a matter of vital importance, if the alkaline carbonates be the only antidotes at hand they should be used unhesitatingly.

ADMINISTRATION.—Sulphuric acid should of course be given properly diluted, and with the requisite precautions to prevent its injuring the teeth. It is best administered in the form either of the *dilute* (*Acidum Sulphuricum Dilutum*—1 to 9, U. S.; sp. gr. 1.082; dose, ten to thirty drops) or of the *aromatic sulphuric acid* (*Acidum Sulphuricum Aromaticum*—1 to 5, U. S.). The last preparation contains alcohol and aromatics. Its dose is from ten to twenty drops.

ACIDUM HYDROCHLORICUM—HYDROCHLORIC ACID. U.S.

Muriatic Acid is a colorless aqueous solution of hydrochloric acid gas, having the specific gravity of 1.160, and containing rather more than 33.9 per cent. of the gas. The muriatic acid of commerce commonly has a yellowish tint, produced by sesquichloride of iron, or sometimes by organic matter.

PHYSIOLOGICAL ACTION.—In its concentrated form muriatic acid is highly corrosive, but less so than either sulphuric or nitric acid. Its astringent properties are not all decided, if indeed it really possess any. As it probably is one of the natural acids of the stomach, it would seem as though it ought to be capable of aiding digestion. It also appears to have influence over the glandular system of the alimentary canal, increasing by its action their normal secretions.

THERAPEUTICS.—In *stomachic dyspepsia*, muriatic acid, with or without pepsin, is often useful by aiding in the digestion of the food. In other cases, where the *dyspepsia* is *intestinal*, with a tendency to diarrhœa and loss of appetite, muriatic acid combined with strychnia and some aromatic, such as compound tincture of cardamom, is often very advantageous. In *low fevers* the use of mineral acids has been highly extolled by various authorities. I have seen a number of cases treated upon this so-called "Swedish plan," and have never been able to perceive that the acids do any real good.

Locally, diluted muriatic acid has been recommended by Bretonneau in *diphtheria*. He employed a mixture of one part of the acid to two of honey; but bolder practitioners have used it of full strength, with, it is claimed, good effect. It should be applied by means of a little mop, scrupulous care being exercised to prevent any of the acid from coming in contact with parts not protected by false membrane.

TOXICOLOGY.—Muriatic acid, as a poison, is similar in its effects to, but less powerful than, sulphuric acid, recovery having occurred after the ingestion of an ounce of the officinal acid (*Boston Medical and Surgical Journal*, vol. xv.). The treatment is similar to that of poisoning from other mineral acids.

ADMINISTRATION.—The acid is best given in the form of the officinal *Acidum Hydrochloricum Dilutum* (℥iv to Oj; sp. gr. 1.038). Dose, ten to thirty drops, properly diluted.

ACIDUM NITRICUM—NITRIC ACID. U.S.

A liquid of the specific gravity of 1.420, which as first made is colorless, but by exposure to the light acquires a yellow tint. It oxidizes all of the common metals except gold, and is exceedingly corrosive to living tissue, which it stains an indelible yellow. When diluted it converts most animal and vegetable substances into oxalic, malic, or carbonic acid.

PHYSIOLOGICAL ACTION.—When applied to any portion of the living organism, nitric acid acts as a most powerful chemical caustic. When very greatly diluted, it is a simple local stimulant, with very slight astringent powers. Owing to its chemical activity, its vapor was at one time used as a disinfectant; but it has been superseded by other substances. Taken internally in small amount, it acts as a stimulant upon the glandular system of the alimentary canal, and in serous diarrhœa appears to exert an astringent influence. It seems to me very probable that these effects are local rather than constitutional, due to a direct action of the acid upon the mucous membrane of the bowel. On entering the blood, nitric acid must be converted into a nitrate. In regard to its elimination we have but little definite information, but it probably escapes through the same channels as does sulphuric acid.

THERAPEUTICS.—Nitric acid is used quite frequently as an escharotic, especially in cases of *chancres* and *venereal* or other *warts*. In its employment care should be taken to protect the sound tissue by oil, or, still better, by a layer of soap. It may be applied by means of a splinter of wood, or, if it is to be used more freely, by a little mop. When it has penetrated as deeply as is desirable, washing the part with warm soapsuds will prevent further action. Very much diluted (five to twenty drops to the ounce), it forms a good stimulant lotion for indolent *ulcers*. It should not be employed as a mouth-wash, on account of its destructive action on the teeth. Of course this does not apply to its use as a caustic in *cancrum oris*, in which, as in other forms of *acute gangrene*, such as *phagedenic chancres* and *hospital gangrene*, it is very efficient. In these cases it must be applied thoroughly.

Internally, nitric acid has been used in *low fevers*, but with doubtful advantage. In *dyspepsia*, in *chronic hepatic congestion*, in the *oxalic acid diathesis*, in the *dyscrasia* of *constitutional syphilis*, nitric acid has been employed with advantage, but is much inferior to the nitro-muriatic acid.

In 1826 Dr. Hope claimed for the *Acidum Nitrosum* a specific action in *serous diarrhœa*, including the sudden acute diarrhœas of hot climates, and in the chronic *dysenteries* originating under similar circumstances. The formula he employed is as follows: ℞ Acidi nitrosi, f ʒi; Misturæ camphoræ, f ℥viii; Misce, et adde Tinct. opii, gtt. xl. S.—A fourth part to be taken every three or four hours. Under the name of *Hope's Camphor Mixture* a preparation similar to this has been much used, but has gradually lost the confidence of the profession, chiefly, I believe, because on theoretical grounds the original formula has been departed from. The *Nitrous Acid* of the shops (*Acidum Nitrosum*, Edinburgh Pharmacopœia) is an orange-red liquid, which may be looked upon as a solution of nitric oxide in nitric acid. When it is diluted with water it is after a short time converted into simple nitric acid. For this reason it has been customary to substitute nitric acid for the Acidum Nitrosum of Hope's original formula. It should be noted, however, that the latter only provided sufficient of the remedy to last a few hours, and, as the reaction which has been spoken of requires some time for its performance, I do not think that theory in truth warrants the change. Practically I have failed absolutely with the new formula, when immediate relief was afterwards obtained by the use of the medicine prepared according to the old plan. Made in this way and used whilst fresh, Hope's Camphor Mixture is a very efficient though disagreeable remedy in diarrhœas connected with disordered secretion of the liver and other glands of the alimentary canal.

ADMINISTRATION.—The dose of the strong acid is from five to twenty drops; of the diluted (*Acidum Nitricum Dilutum*—1 to 6, U. S.; sp. gr. 1.068) from fifteen to sixty drops.

TOXICOLOGY.—When taken in a concentrated form, nitric acid is a corrosive poison, exceeding even sulphuric acid in violence. The symptoms so closely resemble those induced by the latter substance that it is unnecessary to detail them here, as is also true of the treatment. The distinguishing character is to be found in the *color* of the affected tissues, which in nitric acid poisoning are stained of a deep yellow.

ACIDUM NITRO-HYDROCHLORICUM—NITRO-HYDROCHLORIC ACID. U.S.

This preparation is made by mixing three parts of nitric with five parts of muriatic acid. If the acid be sufficiently strong, an orange-colored liquid is formed, with the evolution of intensely-irritating vapors. After standing for a length of time, the *red* color changes to a golden yellow. It is in this state that the United States Pharmacopœia directs the acid to be used. By longer standing the *golden* yellow becomes *lemon*-yellow, and the odor of chlorine is almost entirely lost. These changes are hastened by light, but will occur in the dark and in well-stoppered bottles. Although the golden-yellow acid is directed by the Pharmacopœia, yet careful clinical studies have convinced me that the acid acts much more efficiently when freshly prepared and of a deep-red color. In some cases it has seemed to me useful only when in the latter form. The lemon-yellow acid is nearly valueless.

PHYSIOLOGICAL ACTION.—In concentrated form nitro-muriatic acid is exceedingly corrosive. Our knowledge of its action in small doses is purely clinical, and will be spoken of under the head of Therapeutics. The chemistry of the acid is so complex and uncertain that no reasonable conjecture can be made as to the form in which it is absorbed or the method of its escape from the body. That it is absorbed in some form is proven by its occasionally producing salivation, even when applied to the skin by means of baths.

THERAPEUTICS.—The remedial value of nitro-muriatic acid depends chiefly upon the power which it possesses, to a much greater degree than any other of the mineral acids, of influencing the action of the liver and other glandular organs of the alimentary canal. Originally proposed by Dr. N. Scott, of Bombay, in the *chronic hepatitis* of hot climates, it has been used with great success by Annesley, Martin, and other famous India surgeons. The remedy would seem not to be indicated in hepatitis with high fever and a tendency to rapid suppuration so much as in the slower form of the affection, which normally ends in chronic enlargement and induration of the viscus. In the habitual *congestion* of the *liver* occasionally seen in this climate I have used it with the most marked benefit. In the still milder affection known as "*biliousness*," whose pathology is probably a torpid condition of the small glands of the alimentary mucous membrane as well as of the liver, nitro-muriatic acid has yielded in my hands most excellent results. That the remedy does act upon the liver is proven by the fact that in these cases it sometimes produces violent bilious diarrhœa. When *jaundice* depends upon obstruction or upon any of the severer organic diseases of the liver, the acid is of little if any use; when, however, the jaundice depends upon torpor of the liver, or even when it is catarrhal in origin, the remedy may be of great service. Even in the early stages of *cirrhosis*, whilst the liver is still enlarged, nitro-muriatic acid should be tried, as in some cases apparently of this character great benefit has been derived from its use.

In those forms of *chronic diarrhœa* in which the disease is really an intestinal dyspepsia, nitro-muriatic acid may be of the utmost service, benefiting and even curing cases which have resisted all other treatment. As the effect of the acid is not a sudden one, it is evident that it acts in these cases not as an astringent, but by restoring the normal digestive power.

There is a morbid condition, probably dependent upon defective primary assimilation, in which the chief symptoms are general malaise, a feeling of weakness, a lack of elasticity, a very great depression of spirits, in which crystals of oxalate of lime are generally to be found in the urine, and in which nitro-muriatic acid produces in a few days a surprising revolution.

As a "blood-purifier" the acid has been employed in *constitutional syphilis*, and in various ulcerative *skin-affections*. In these diseases it no doubt does good by improving digestion and increasing glandular action, but there is no reason to believe that it is a direct alterative.

ADMINISTRATION.—For reasons which have already been given, when nitro-muriatic acid is administered internally it should be freshly prepared; and, as the changes which have been spoken of take place more rapidly when the acid is mixed with water, the officinal *dilute* nitro-muriatic acid is an ineligible preparation. As light hastens its deterioration, the strong acid should always be kept in a dark bottle with a glass stopper. Directly after mixing the acids the evolution of gas may be so great as to necessitate its being allowed to escape. After six or eight hours, however, the bottle should be closely stoppered. The dose of the strong acid is from five to eight drops, properly diluted, and taken through a tube after meals.

In *chronic hepatic diseases* the external application of the acid seems to give even better results than its internal use. In India, according to Sir Ranald Martin, the bath is used as follows: 1. Take Hydrochloric acid f℥iii, Nitric acid f℥ii, Water f℥v. Mix. Two gallons of water and six fluidounces of the above mixture suffice for a bath, which will keep fit for use during three days, provided half a fluidounce of acid and a pint of water are added morning and evening. The bath must of course be given in wooden or earthenware vessels, and if it becomes necessary to warm it only a portion should be heated, and the rest then added. In urgent cases the whole body may be immersed in the bath; but generally a foot-bath is preferable, the inside of the thighs and arms and the hepatic region being at the same time sponged. The bath should be repeated twice daily, lasting each time for ten or fifteen minutes.

I have had no experience in this method of using nitro-muriatic acid, but have derived great benefit from the application of the acid over the hepatic region. My plan has been to wring out a large piece (eight by ten inches) of spongio-piline, or of canton-flannel (several layers), in a lotion of a strength varying, according to the irritability of the patient's skin, from one to three fluidrachms to the pint, and to apply this over the right hypochondrium, covering it with a piece of oiled silk supported by a bandage. The application sometimes causes a prickling sensation, and after a time may produce a profuse local sweating. The dressing may be left on from half an hour to an hour, and be repeated three or four times a day; some patients can wear it almost continuously.

TOXICOLOGY.—When taken in poisonous doses, nitro-muriatic acid produces symptoms and results similar to those following the ingestion of nitric acid. The color of the stain produced by it is yellow, and its antidotes are the same as those of other mineral acids.

LACTIC ACID (ACIDUM LACTICUM, U. S.) appears to be the natural acid of the gastric juice, and may with propriety be used as an adjuvant to pepsin in doses of half a drachm three times a day. W. Preyer, conceiving that sleep is due to the presence in the blood of the results of tissue change, amongst which is lactic acid, experimented with it and its soda salt, and announced that they acted as powerful soporifics upon both man and the lower animals (*Centralb. Med. Wissens.*, 1875, p. 578). According to his statements, with the sleep came deep, slow respiration, with lessening of reflex activity and of the bodily temperature. Subsequent papers by Dr. E. Mendel (*Deutsch. Med. Wochens.*, 1876, No. 17), Dr. Erler (*Centralb. Med. Wissens.*, 1876, p. 658), Dr. Fischer (*Lond. Med. Record*, 1877, p. 193), Dr. Lothar (*Virchow's Archiv*, Bd. lxvi. p. 120), and Dr. Senator (*Berlin. Klin. Wochens.*, 1877, p. 537), have shown that the hypnotic powers of lactic acid and its salts are very feeble and uncertain. The large doses used also are very prone to produce irritation of the alimentary canal, and Senator noticed the production of rheumatic pains. From three to nine drachms of the lactate of sodium may be given at a dose.

PHOSPHORUS. (P.) U.S.

Phosphorus is a translucent, when pure nearly colorless, but usually slightly yellowish, highly inflammable elementary body, which is tasteless, but possessed of a peculiar alliaceous odor. It is obtained from the phosphate of calcium of calcined bones, by taking away the lime with sulphuric acid and deoxidizing the residuum by heating with charcoal. It is insoluble in water, sparingly soluble in ether, absolute alcohol, and the oils, freely so in chloroform. It takes fire at 100° F., and melts at 108° F. In the shops it is in cylindrical sticks, covered with a whitish layer, and having when cut a waxy consistence and lustre. When properly treated, it is converted into several allotropic forms, the red phosphorus, black phosphorus, and the crystallized metallic phosphorus of Hittorf. The first of these is the most important; it is brittle, does not take fire at ordinary temperatures, and is said not to be poisonous.

PHYSIOLOGICAL ACTION.—The physiological action of phosphorus in therapeutic doses is probably entirely different from that which it exerts when in larger amounts. It is a constituent of most of the more important tissues, and is especially abundant in the nerve-centres. Like iron, cod-liver oil, etc., it appears to act when given in minute quantity as a stimulant to the nutrition of the tissues, into whose composition it enters. So far as the nervous system is concerned, this assertion rests chiefly upon clinical observation; but Dr. Wegner (*Virchow's Archiv*, June 22, 1872) has experimentally demonstrated such an action upon the bony tissues. He found that when adult animals were fed upon minute doses of phosphorus the spongy tissue in the long and short bones was thickened, and the compact tissue rendered more dense. After a time new tissue was deposited upon the inside of the shafts of the long bones, in some instances until the marrow-cavity was obliterated. The action upon the bones of growing animals was even more marked.

Phosphorus was at one time believed to be a diffusible stimulant, and it possibly may exert such an influence. In the acute nervous exhaustion of *typhoid pneumonia* I have seen it apparently act very favorably in this way.

For reasons to be hereafter adduced, it is certain that in poisonous doses phosphorus acts as phosphorus, and when it is administered therapeutically it certainly enters the blood in its elemental form, and, I believe, acts as such. Dr. Wegner advances the following reasons for believing that it does not act as phosphoric acid so far as the bony tissues are concerned. First, no similar action can be obtained from phosphoric acid unless from eight hundred to one thousand times the proportional dose be given. Second, the newly-formed tissue is at first gelatinous. Third, there is no excess of phosphates in the bone. Fourth, when the food is deprived of lime the same new tissue arises, but remains in a soft, gelatinous state.

THERAPEUTICS.—The chief use of phosphorus in medicine is as a nutrient tonic to the nervous system. In all cases of chronic *nervous exhaustion*, whether involving the cerebral or spinal centres, it is of great value. I have seen marked benefit from its use when the symptoms were not severe enough to indicate organic lesion; but the most remarkable results have been in the cases in which the structure of the centres was apparently deeply implicated. In threatening *cerebral softening*, in *myelitic paraplegia* from excessive venery, it is the only drug which appears really to affect the nerve-centres.

In *neuralgia* attention has recently been drawn by several writers to its virtues; and, as neuralgia is often simply an expression of exhausted nerve-power, the use of phosphorus is commended by reason as well as by experience.

It is probable that it may be of value in some cases of impaired vitality, although the nervous system be not obviously implicated. Dr. H. Eames (*Dublin Journal of Medical Sciences*, Jan. 1872) states that he has obtained great benefit from its use in obstinate skin-affections, such as *lupus*, *acne*, and *psoriasis*. Attention has been recently called abroad to its use in *cataract*.*

On account of its marked influence on the development of bone, Dr Wegner suggested its use in *osteomalacia* and in *rickets*, and Dr. Friese states (*Berlin. Klin. Woch.*, 1877, p. 437) that he has had brilliant success from its use in combination with iron in several cases in which ordinary treatment had failed. The recent elaborate article of M. Kassowitz (*Zeitschrift. Klin. Med.*, 1884, 115) confirms this specific action of phosphorus, and I think it should be persistently administered to all rachitic children. Prof. Samuel R. Percy has used phosphorus successfully for repeated *furuncular* eruptions (*Prize Essay*, *Trans. Amer. Med. Assoc.*, 1872, p. 659).

TOXICOLOGY.—The ingestion of a fatal dose of phosphorus is not followed by any sensible effects for some time. After, however, from three to twelve hours a sense of weakness and of general wretchedness manifests itself, and in a large proportion of the cases (according to Lewin eighty-eight per cent.)

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* Dr. Tavignot, *Revue de Thérapeutique Médico-Chirurgicale*, August and September, 1871; Prof. Gioppi, *Giornale d'Oftalmologia*, abstract in *N. Y. Medical Record*, 1872.

is accompanied, or soon followed, by vomiting. With the emesis there is nausea, and in most cases the patient soon complains of abdominal pain, the severity of which, however, never equals that of corrosive poisoning. The matters vomited consist of food, mucus, and bile. During the first eight or ten hours they often smell strongly of phosphorus, and are luminous in the dark. The vomiting may persist during the whole attack, but generally ceases on the second or third day, to reappear with the subsequent jaundice, when coffee-colored vomit from exuded blood is ejected. The pain, which in most cases abates with the vomiting, often spreads from the epigastrium over the whole abdomen, and in rare instances is paroxysmal. If it reappear in the latter stages, it is apt to affect especially the right hypochondrium, and is associated with decided tenderness in the region named and in the epigastrium.

The tongue is whitish or abnormally red, sometimes furred. There is generally fever, loss of appetite, and thirst. Maukopff has noted a morning and evening temperature of from 37° C. to 39° C., and from 37.4° C. to 39.8° C. respectively. During the latter part of the case there is very often a remarkable fall in the temperature, which is generally, but not always, a precursor of death. The lowest point I have seen noted was 31.2° C. (88.2° F.) some hours before death.* In some cases fever is altogether absent or comes on just before death.†

The stools are at times normal in character and frequency, but there is generally diarrhœa or constipation, with flatulence. Late in the attack the passages are in most cases very light clay-colored, or even whitish, and exceptionally they are bloody. In some cases they are phosphorescent.

Jaundice comes on in from thirty-six hours (cases reported by Maukopff, *Wiener Medizin. Wochenschrift*, 1863, and by Tüngel, *Klinische Mittheilungen von der Medicin. Abtheilung des Allgemein. Krankenhauses in Hamburg*, 1861) to five days (Lebert and Wyss, *Archives Générales*, 6th series, xii., September, 1868) after the ingestion of the poison. In most cases it appears first in the conjunctiva, but sometimes the urine gives previous warning of its approach. In some cases there is with it a decided and palpable increase in the size of the liver, which may pass, if the patient live long enough, into an equally apparent lessening of the bulk of the viscus. The severe nervous symptoms are rarely if ever developed until after the jaundice, although early in the attack there is not unfrequently anxiety, headache, giddiness, and dreamy unquiet sleep, or even sleeplessness. The more pronounced nervous symptoms consist of delirium, which may be wild and is very frequently erotic, with somnolence ending in coma and death, occasionally preceded by convulsions. According to Taylor, the latter are a certain sign of approaching dissolution. Very generally, partial spasms and fibrillar contractions of the voluntary muscles occur, although there is always, in not too rapid cases, progressive paresis of the voluntary muscles. Death is usually put off beyond twenty-four hours, yet it has occurred in a child in four hours, and in the adult in seven hours after the ingestion of the poison (*Wiener Med. Wochensch.*, May, 1884, 608). The patient may suddenly succumb to collapse and cardiac paralysis, but more commonly he dies comatose from a gradual failure of the respiration and circulation.

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* See case of Dr. Battmann, *Archiv der Heilkunde*, 1871, p. 257.

† See case of Concato, *Sydenham Soc. Year-Book*, 1869–70, p. 454.

If recovery occur, it is by a gradual amelioration of the symptoms, and the health of the patient is apt to be impaired for some time. Apparently desperate cases will sometimes convalesce unexpectedly, and Tüngel states that a favorable issue may take place even after violent delirium.

The urine is almost always much affected by the poison. Very commonly it is scanty, is albuminous, and sometimes it contains sugar. As was first pointed out by Munk and Leyden (*Die acute Phosphorvergiftung*, Berlin, 1865), after jaundice has set in, bile-acids, as well as biliary coloring-matter, are always to be found in the urine. Not unfrequently a cloudy sediment consisting in part of epithelial cells, often tinged with bile, is deposited. Dr. Oswald Kohts (*Pflüger's Archiv*, Bd. iii. p. 1) and other observers have found leucin and tyrosin in the urine of dogs poisoned with phosphorus, and undoubtedly these substances are sometimes to be met with in the human excretion. The albuminuria generally follows, but may precede, the icterus. A very remarkable and apparently constant constituent of the urine is the sarco-lactic acid. Fat has been found in the urine inside of renal epithelial cells, and also as free globules (Schütz, *Prag. Med. Wochenschrift*, 1882, vii. 322).

Phosphorus induces in animals symptoms parallel with those commonly seen in man; although Kohts states that he has seldom seen albuminuria in animals, even when the structure of the kidneys was profoundly altered. Orfila, Magendie, Munk, and Leyden found that the only effects following the injection of phosphuretted oil into the jugular vein of an animal were the exhalation of phosphoric acid and broncho-pulmonary inflammation: on examination (Munk and Leyden), oil, but no phosphorus, was found in the lungs. Ludimar Hermann and Alfred Brunner (*Deutsch. Archiv für Klin. Med.*, p. 198) have shown that in these experiments there was embolic arrest of the oil in the pulmonary capillaries, and consequent inflammation with subsequent oxidation of the phosphorus. When the phosphuretted oil is injected in the form of a fine emulsion, the characteristic symptoms and post-mortem appearances of phosphorus-poisoning result.

In some instances phosphorus-poisoning presents symptoms quite different from the typical array. Death may take place in a few hours, and in such cases jaundice is not generally present (case, *London Lancet*, 1879, ii. 311). Zeidler reports a death in forty-two hours, from suppression of urine, with collapse and erotic delirium. In a case of Bollinger's (*Deutsches Archiv für Klin. Medicin*, Bd. vi., 1870) the chief symptoms were vomiting, pain and tenderness over the abdomen, great weakness of pulse, gradually-developed paralysis of the legs, and death, without jaundice, in four and a half days. The autopsy revealed hemorrhagic effusion between the membranes and the spinal cord, and also into the sheaths of the proximal portions of the spinal nerves.

In women, fatal doses of phosphorus very commonly produce a bloody pseudo-menstrual discharge, and when pregnancy exists almost invariably induce abortion or miscarriage. M. Miura has found in the foetus of poisoned rabbits structural changes similar to those of the mother (*Virch. Arch.*, xcvi. 54).

The older toxicologists spoke of an erosive gastritis as a common result of phosphorus-poisoning, but it is now well established that such affection is very rarely induced by the drug.[*] As was first pointed out by Virchow (*Virchow's Archiv*, Bd. xxxi., 1864) there is universally a gastro-adenitis, which causes the gastric mucous membrane to be thickened, opaque, whitish, grayish, or yellowish-white. Under the microscope the epithelial cells appear swollen and filled with granules and oil-globules, and in very advanced degeneration the cells completely break down. This gastro-adenitis is not due to a local action of the phosphorus, because it occurs when the poison is introduced through other channels than the mouth. The duodenum and intestines suffer similar changes. The liver is generally very much enlarged, friable, and light-colored; sometimes it is mottled, and sometimes portions of it are deeply stained with bile.[†] The cells are gorged with fat-globules,[‡] and in some cases there are small-celled interstitial thickenings due to hyperplasia of the trabecular tissue. The gall-bladder may be full or empty. In protracted cases the liver undergoes atrophy, with destruction of its secreting cells. The kidneys, especially in their cortical portion, suffer a degeneration similar to that of the liver, the epithelium becoming enlarged, granular, fatty, and finally undergoing destruction. The voluntary and cardiac muscles, the spleen, the lungs, and probably all the tissues, partake of the universal fatty degeneration* which Wegner has shown to involve even the minute arterioles.

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[*] It would appear probable that if it occurred at all it would be in rapidly fatal cases; yet Tüngel did not find it in a patient dead in nine hours of phosphorus-poisoning.—*Virchow's Archiv*, Bd. xxx., 1864.

[†] According to researches made by Dr. Emile Rousseau in the Pathological Laboratory of the University of Pennsylvania, the first anatomical changes in the liver occur in the centre of the lobules around the hepatic vein.

[‡] A. Lebedeff (*Arch. f. Physiolog.*, xxxi. 11, 1883) believes that the fat in the liver is not produced by degeneration of the hepatic tissue, but has simply been transported there from the subdermal regions. He bases this opinion upon his own observations,—first, that the phosphorus fat has the same chemical constitution as has the subdermal fat; second, in a dog which had been fed with linseed oil and then poisoned with phosphorus, the liver was loaded with linseed oil. This evidence is of very little value, because on the one hand the linseed oil probably accumulated in the dog's liver before the poisoning and simply remained over, and on the other hand there is no proof that fat produced by degenerative changes necessarily differs in composition from other fat. The fact that the liver and other organs are destroyed in phosphorus-poisoning may be considered proof that the fat is formed out of the affected tissue.

The blood is often profoundly affected, becoming very dark, losing its power of coagulation, and apparently suffering also in its corpuscular elements; for ecchymoses are almost universal, and hæmatin crystals are occasionally found in the viscera. In the case of Concato (*loc. cit.*) the white corpuscles were observed during life to be increased in number, and the red to be diminished in size and altered in form. The ecchymoses occur in all parts of the body, but are apt to be especially pronounced in the mediastinum and the serous membranes. Schiff has found that in dogs, after death from phosphorus, the blood does not pass into the veins, but remains in the arteries (*Archiv für Exper. Pathol. und Therap.*, Bd. ii. p. 347).

Dr. Mayer states that when very large doses of the poison have been taken, the blood and even the urine (?) may be phosphorescent (*Canstatt's Jahresbericht*, Bd. v., 1862, p. 123).

The elimination of bile-acids in the urine shows that the jaundice of phosphorus is caused not by an arrest of secretion, but by an occlusion of the biliary passages and consequent resorption of the bile. Dr. O. Kohts (*loc. cit.*) has apparently demonstrated that the occlusion is most frequently due to the duodenitis involving the common duct, so as to obliterate its lumen by the swelling of the mucous membrane. In some cases, however, it is probable, as believed by Wyss, Alter, and Ebstein, that a catarrhal inflammation of the minute gall-ducts is the cause of the jaundice, and also that the result is in part effected through pressure upon those ducts by the swelling of the glandular and trabecular tissue.† It is proper to state that Demarbaix and Willmart (*Presse Médicale*, xxi., 1869, and *Schmidt's Jahrbücher*, p. 152, Bd. cxliv.) insist that the icterus is not really heptogenous, but hæmic in origin, chiefly because they have found hæmatoidin in the urine. This fact, however, proves only that the blood is altered by the poison: it does not disprove the liver-origin of the jaundice.

Acute phosphorus-poisoning so closely resembles yellow atrophy of the liver that their clinical distinction is sometimes difficult, nay, impossible. Distinct phosphorescence in the breath, vomit, or stools would of course be direct evidence of poisoning. This phosphorescence, however, very often cannot be detected: according to Vetter (*Virchow's Archiv*, Bd. liii. p. 186) it can be rendered more evident in the vomit, stools, etc., by acidifying with sulphuric acid and warming in a shallow dish. When death ensues during the first week of phosphorus-poisoning, the enlarged liver affords a distinctive proof of poisoning; but when the case is more protracted, the atrophied liver of phosphorus cannot be distinguished from that of the natural disease. The symptoms during life rarely, if ever, afford sufficient ground for a positive diagnosis. The lull in the symptoms after the first onset of the disease happens more generally in phosphorus-poisoning than in yellow atrophy. Yet the clinical differences between various cases of either affection are greater than those which have been relied upon as separating the two affections. Köhler has asserted that oxymandelic acid in atrophy of the liver replaces the sarco-lactic acid of phosphorus-poisoning, and stress has been laid upon the asserted facts that in the natural disease leucin and tyrosin are present in abundance in the urine, whilst in the poisoning they are absent. In yellow atrophy, however, tyrosin is not unfrequently absent from the urine, and leucin present in very small amount, whilst both principles may be present in phosphorus-poisoning.* In regard to the acids in the urine, very careful chemical analysis would in any case be necessary to determine their presence, and sufficient evidence is certainly not yet forthcoming to show that either of them is really characteristic. Chemical examination is therefore absolutely necessary in all medico-legal cases. (For discussions of the diagnosis between yellow atrophy and phosphorus-poisoning, see Köhler, *Sydenham Year-Book*, 1870, p. 455; Schultzen and Ries, *Annalen des Berlin. Krankenhauses*, Bd. xv., 1869; and especially Dr. I. Ossikovsky, *Wien. Medizin. Presse*, xiii., 1872, abstracted in *Schmidt's Jahrbücher*, Bd. cliv. p. 15. For cases in which the question was legally raised, investigated, and discussed, see *Schmidt's Jahrb.*, Bd. cxli. p. 167; *Syd. Year-Book*, 1832, p. 430; *Annales d'Hygiène*, Jan. 1869.) According to M. Poulet (*Gaz. Méd. de Paris*, Aug. 1872) phosphorus is eliminated as hypophosphoric acid, and the poisoning can be recognized by heating the urine with nitric acid to calcination. If hypophosphoric acid be present, as dryness is reached the mixture suddenly bursts into a flame like a packet of matches.

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* The scope of the present work does not allow of a full discussion of the pathology of phosphorus-poisoning. The reader is referred to the following papers: *Études cliniques et expérimentales sur l'Empoisonnement aigu par le Phosphore.* Par Prof. H. Lebert et Dr. O. Wyss.—*Archives Générales*, Sept. 1868. *Zur pathologischen Anatomie der acuten Leberatrophie und der Phosphorvergiftung*, von Dr. Otto Bollinger.—*Deutsches Arch. f. Klin. Med.*, Bd. v., 1869. *Ueber Icterus bei Phosphorvergiftung*, von Dr. O. Kohts.—*Ibid.*

† For an elaborate discussion of the cause of jaundice, see Kohts's Memoir, *Deutsches Archiv*, Bd. v. p. 168; consult also that of Dr. Bollinger, *Centralblatt für die Med. Wiss.*, 1869, and *Deutsches Archiv*, Bd. v., 1869.

It has of late years been demonstrated that phosphorus passes into the blood as phosphorus, and not in the form of phosphoric acid or other compound. In poisoning-cases in men the breath is said sometimes to be distinctly phosphorescent; and in animals Bamberger has found phosphorus in the blood, and Husemann and Marme in the liver, two or three hours after its ingestion; W. Dybkowsky (*Hoppe-Seyler's Medicinisch-chemische Unter-*

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* Cases (*Wiener Med. Presse*, 1872; *Schmidt's Jahrb.*, Bd. 169, p. 127; Bd. 195, p. 123). Prof. Ossikovsky believes that the principles appear habitually about the sixth day of the poisoning, when the liver is still enlarged.

suchungen, Heft i. p. 54) has detected it in the blood and liver ten hours after its ingestion; and other observers have demonstrated its presence in almost all of the tissues. It seems probable that to some extent it finds entrance into the circulation by being dissolved in the various fatty matters contained in the alimentary canal. At the temperature of the body, however, it yields abundant vapors, and Bamberger has demonstrated that these readily and rapidly pass through animal membranes. He has found that defibrinated blood, when separated from the fumes of phosphorus only by an animal membrane, rapidly becomes saturated with the poison. Dybkowsky (*loc. cit.*) has confirmed this, and it cannot be doubted that in a similar manner living blood absorbs the poison from the alimentary canal.

W. Dybkowsky (*Hoppe-Seyler's Medicinisch-chemische Untersuchungen*, Heft i.) renders probable the theory of Schuchardt (*Henle und Pfeufer's Archiv*, N. F., Bd. viii.) that the phosphorus to some extent in the alimentary canal, but much more largely in the veins, is converted into phosphuretted hydrogen, and that some of this compound and some of the phosphorus itself is oxidized in the venous blood, so that phosphoric acid, besides phosphorus and phosphuretted hydrogen, is emptied into the arterial blood; further, that the last two compounds are oxidized at the expense of the arterial blood and the tissues it feeds, and that the poisoning is due to this deprivation of oxygen. For the details of the experiments upon which these conclusions rest I must refer the reader to the original memoir.*

The indications for treatment in phosphorus-poisoning are very evident It is plain that no medication can influence the terrible organic lesions induced, and that the primary object must be to prevent the absorption of the poison. Emetics and purgatives are, therefore, of prime importance. The necessity of the persistent use of evacuants is shown by the finding of phosphorus by Dr. Starck in the stools three and a half days, and in the vomit two days, after the ingestion of the fatal dose (*Deutsches Archiv Klin. Med.*, Bd. xxxv. 482). As phosphorus is soluble in oils, *no fatty matters* should be allowed either in the food or medicines. As an emetic, *sulphate of copper should always be chosen.*

The minute particles of phosphorus adhere so closely to the alimentary canal that they cannot be dislodged by mechanical means, and an antidote is urgently demanded. For the purpose of oxidizing the poison, Duflos suggested magnesia usta and liquor chlorini, and Scherer the chloride of lime; but in practice these substances have been found of no value, on account of the slowness of their action.

The oil of turpentine, originally proposed by Andant (*Journal de Méde-*

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* M. Leoorché (*Archives de Physiologie normale et pathologique*, tome i., 1868, tome ii., 1869) believes that phosphorus acts in the blood as phosphoric acid, but does not establish his opinion. For a discussion of this, see Dybkowsky's paper.

cine de Bruxelles, 1868–69) as an antidote to phosphorus,* has been largely used by experimenters, with apparently contradictory results, which, as is now known, were due to the employment of different varieties of the oil. There are in European commerce three varieties of turpentine,—the rectified, the German, and the French. Jonas (*Liebig und Wöhler's Annalen der Chemie*, Bd. xxxiv.) found that whilst the pure oil has no effect upon phosphorus, the acid French oil forms with it a crystalline, spermaceti-like mass. This is soluble in ether, alcohol, and alkaline solutions, and has received the name of turpentine-phosphoric acid. It is said to be eliminated by the kidneys unchanged, and to exert no deleterious influence. The elaborate experiments of Vetter on dogs and rabbits gave results in accord with these facts, for he found the rectified and German oils to be of no value in phosphorus-poisoning, whilst the crude acid French oil was distinctly antidotal. Koehler, however, asserts that when the German oil has not been rectified for some time, it acts upon phosphorus. He believes that the oil acts partly by oxidizing the poison, and partly by converting it into the harmless turpentine-phosphorous acid. One part of the oil must be given for 0.01 part of the phosphorus. (*Detroit Review*, 1873; from *Med.-Chirurg. Rundschau*, June, 1873. Case of recovery, *Guy's Hosp. Reports*, xxvi. 13.) Neither ordinary American oil of turpentine nor Canada balsam are of value in phosphorus-poisoning

As was pointed out by MM. Eulenberg and Guttmann (*Aertz. Literaturblatt*, 1868, No. 12, quoted in *Sydenham Year-Book*, 1868, p. 450), and subsequently by Prof. Bamberger (*Wiener Medizinische Presse*, Jan. 1872; *Virchow's Archiv*, June, 1872), phosphorus in a solution of a soluble salt of copper becomes immediately black, owing to the formation of a phosphide of the metal. Prof. Bamberger (*loc. cit.*) also asserts that, whilst this change is very rapid, that induced by turpentine is a slow one, and, from an elaborate series of experiments upon animals, concludes that copper is much the more valuable and certain antidote. In human poisoning, then, sulphate of copper should be given in dilute solution, three grains every five minutes until vomiting is induced. After this, if the French oil be accessible, it may be given freely in emulsion. Otherwise, sulphate of copper, with opium to restrain the emesis, should be administered in such doses as the stomach will retain. Sulphate or citrate of magnesium should be used as a quickly-acting purge, and symptoms as they arise should be judiciously treated.

Matchmakers and other artisans who are exposed by their occupations to the fumes of phosphorus suffer from chronic poisoning, which, whilst in many cases it profoundly affects the vitality of the sufferer, is especially distinguished by the occurrence of necrosis of the upper or lower jaw. It has long been known that those artisans who have bad teeth are especially liable to be seriously affected, and the experiments of Wegner have demonstrated that the necrosis of the jaw is due to the local action of the vapor of phosphorus upon the part. He found that when rabbits were kept in an atmosphere full of the fumes of the poison no necrosis ever occurred, unless, by means of an unsound tooth or an artificial wound, the atmosphere had access to the bone. If such access were, on the other hand, allowed to any bone of the body, periostitis and subsequent necrosis resulted. Further, when rabbits received continuously small doses of the phosphorus by the mouth, no necrosis occurred even after wounds which laid bare the bones. As phosphorus-necrosis belongs to the province of the surgeon rather than of the physician, I will not discuss it further here.

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* For cases, see *Gazette Hebdomadaire*, 1874; *Schmidt's Jahrbücher*, Bd. 169, p. 126; *Med. Times and Gaz.*, 1876, ii. 461.

ADMINISTRATION.—Phosphorus may be given in pill or in solution. The *Oleum Phosphoratum*, U. S., containing one per cent. by weight of phosphorus, may be given in doses of one to three minims in aromatized emulsion or in capsules. The *Pilulæ Phosphori*, U. S., or officinal pills of phosphorus, contain one-hundredth of a grain each. In regard to the dose of phosphorus, I have found that many stomachs will not bear more than the fiftieth or even the hundredth of a grain, as given in the liquid form; but I have often given as high as the twentieth of a grain. Dr. J. A. Thompson has used it in much larger doses (*London Practitioner*, July, 1873), prescribing one-twelfth of a grain as an average dose, and in one case having given as high as one-fourth of a grain every four hours without injury. On the other hand, Dr. Anstie has seen slight poisoning from three-fourths of a grain taken in small divided doses during seven days (*London Practitioner*, Aug. 1873).

ZINCI PHOSPHIDUM, U. S.—*Phosphide of Zinc* has been largely used with asserted good results as a substitute for phosphorus. According to the researches of Vigier (*Bull. Thérap.*, xc., Jan. 1876) it would seem that the phosphide yields its phosphorus within the economy, probably to form a phosphuretted hydrogen. He found that it killed rabbits more quickly than did a corresponding dose of phosphorus, and that both symptoms and lesions were identical in the two cases. The phosphide should be given in pill or granule. The dose may be considered as one-twentieth to one-twelfth of a grain. Prof. Seguin recommends doses of from one-fourth to one-sixth of a grain.

CLASS III.—CARDIAC STIMULANTS.

THE term cardiac stimulants is here used to designate a number of medicines which, when given internally, increase the power and force of the circulation, and are used by the physician for such purposes. There are some substances which are heart-stimulants in reality, but which possess other properties in so great a degree as to overshadow their cardiac relations, and are not used by the physician to affect the circulation. Such medicines are considered in connection with those powers which give to them their clinical value, and are consequently not included in the present class. Some of the members of this class are slow in their operation, some more rapid. Some produce increase in the pulse-rate, some lower it. It is evident, then, that no general indications can be laid down for their use, but that medicines so diverse must be studied individually.

AMMONIA.

Ammonia is a colorless, irrespirable, highly irritant gas, of a strong alkaline reaction, extremely soluble in water. It is obtained upon a large scale as a waste product in the manufacture of coal gas, and is officinal in the Materia Medica list of the U. S. Pharmacopœia in the form of the stronger water of ammonia, and the muriate, carbonate, nitrate, and sulphate of ammonium.

PHYSIOLOGICAL ACTION.—Locally applied, ammonia is a very powerful irritant. When inhaled, it causes intense irritation, and finally inflammation of the mucous membrane of the air-passages, and its solution, if kept in contact with the skin, reddens, blisters, and at last produces even sloughing of the parts. When ammonia is injected into the veins of animals in considerable quantities, it causes violent convulsions, with remarkable disturbance of the respiration, followed, if the dose has been large enough, by death in a very short time. (F. Lange, *Archiv für Experiment. Pathol. und Ther.*, Bd. ii. p. 368; V. Feltz et E. Ritter, *Journal de l'Anatomie et de la Physiol.*, 1874, p. 326; Funke, *Pflüger's Archiv*, Bd. ix. p. 426.) The respiration, if not interfered with by the tetanus, is enormously accelerated. Billroth (*Archiv für Klin. Chirurg.*, Bd. vi. p. 421) states that the temperature falls enormously in animals poisoned with ammonia.

Respiration.—Where a small quantity of ammonia is injected into the blood of an animal, the breathing is greatly accelerated; after larger doses a period of arrest of respiration occurs in expiration (Funke), at once or in the course of a few seconds, and precedes the hurried breathing. In regard to the effect of section of the pneumogastrics upon the respiratory action of ammonia there is some disagreement: thus, in Funke's observations the primary arrest of respiration was always present, whilst in the experiments of Lange it was always absent. Both observers note, however, that section of the pneumogastrics does not interfere with the increased rapidity of the breathing, and Funke especially remarks that the change from the slow, deep breathing of divided vagi to the extremely rapid respiration of ammonia-poisoning is colossal. Our knowledge of the physiology of respiration is hardly sufficient to warrant a positive deduction; but the facts noted indicate very strongly that ammonia is an intense direct stimulant to the respiratory centres in the medulla oblongata.

Circulation.—The chief practical interest in the physiological action of ammonia centres in the circulation. It is chiefly as an arterial stimulant that it is used in medicine, and clinical experience assigns to it a powerful but fugacious action on the heart. The only experiments on the subject besides my own that I have met with are those of Lange. When the drug is injected into the veins of animals there is a momentary fall of the arterial pressure, followed by a sudden, decided rise, and a corresponding increase of the pulse-rate. These phenomena are independent of the convulsions, because, in Lange's experiments, they occurred in curarized animals. According to Lange's studies the rise of pressure is not due to any stimulation of the vaso-motor centre, because it took place equally after division of the cord,—*i.e.*, after the separation of the arterioles from the vaso-motor centre. The increased arterial tension which follows the exhibition of ammonia must therefore be due to an action either upon the heart itself, or upon the peripheral vaso-motor nerve-fibres, or upon the muscular fibres in the coats of the arteries. As in Lange's experiments the increase of the pulse-rate did not accompany the rise of pressure after section of the spinal cord, it would seem to be caused by a stimulant action upon the accelerators of the heart, which are of course paralyzed by spinal section. The fall of arterial pressure, which immediately follows the injection of ammonia into the jugular vein, is probably due to a direct action of the concentrated poison on the heart. Previous section of the vagi does not prevent it, and when the dose is sufficient it is replaced by permanent diastolic arrest of the heart's action. That it is not produced by spasm of the pulmonic arteries is shown by the fact that when death occurs the left heart is found full of blood. When administered in toxic doses, ammonia, probably, has some effect upon the hæmic corpuscles, for Feltz and Ritter found that the blood of a dog killed by the poison not only did not contain anything like the normal amount of oxygen, but even when shaken up with the gas refused to absorb it; further, under the microscope the red disks were found to resist the action of acetic acid to a markedly abnormal degree.

Motor System.—The convulsions already spoken of as being produced by ammonia are not cerebral, since Lange found that they occur equally after division of the cord; nor are they peripheral, since, in Funke's experiments, tying of the artery of a limb failed to arrest them in that part, whilst section of the nerve was followed by immediate quiet: they must be spinal. Ammonia, in toxic doses, acts, therefore, as a stimulant to the motor function of the spinal cord, heightening, as has been proven experimentally by Funke, its reflex activity.

Elimination.—The volatility of ammonia and the extreme fugaciousness of its action would seem to indicate its elimination by the lungs; but Feltz and Ritter (*loc. cit.*, p. 323) failed to find it in the breath of a poisoned animal, and the researches of H. Bence Jones apparently demonstrate that at least a portion of it is oxidized in the system (*Philosophical Transactions*, London, 1851). The last observer found, to his surprise, that even large doses, far from increasing the alkalinity of the urine, seem at times to heighten its acidity. It occurred to him that the ammonia might be oxidized; and he accordingly found that the natural product of its oxidation, nitric acid, appears in the urine after the exhibition either of the ammonia itself or of its tartrate, carbonate, or muriate. It is probable that some portion of the ammonia is, in conjunction with carbonic acid, converted into urea.*

THERAPEUTICS.—Externally, ammonia is much used as a constituent of irritating liniments, and, on account of its efficiency and cheapness, is very valuable. By inverting a watch-glass full of the stronger water of ammonia upon the skin, a blister may be raised in a very few minutes; but, as the effects of the application are very apt to be severe, the use of it is justifiable only under rare circumstances.

Internally the chief indication for the use of ammonia is *failure of the heart's action.* The more sudden and purely functional this is, the more efficacious is the remedy, which should in such cases be not only administered by the stomach, but should also be inhaled through the nostrils, as the local action of the irritant vapor upon the mucous membrane has a very arousing influence. When the failure of the circulation depends upon a slow and persistent cause, as in *adynamic fevers*, ammonia is not generally useful, but may be employed as an adjuvant to alcohol in the crisis of the disorder.

In *poisoning by venomous serpents*, ammonia has been largely used, but certainly is in no sense antidotal, since, according to the experiments of Dr. Fayrer (*Indian Annals of Medical Science*, 1872), mixing it with the poison before injecting the latter into an animal does not in any way delay the fatal result. As an adjuvant to other more powerful stimulants, and especially to alcohol, ammonia may be useful in these cases. Dr. G. B. Halford, of Melbourne, Australia, has claimed (*Melbourne Argus*, 1872) that when injected into the veins its effects in poisoning from snake-bite are very extraordinary, and several cases of recovery after its use in this manner have been reported. It is far from certain, however, that these cases would have died had no medication been practiced; and Dr. Fayrer states that in an extended series of experiments upon animals he has not found its injection to be of any use. Ammonia cannot, therefore, be considered a specific in snake-poisoning; but, as the injection can do no harm, it should be practiced, yet never to the exclusion of other measures.

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* The relation of ammonia to the formation of urea is of such purely physiological interest, and its discussion would require so much space, that I dismiss it with the following references, which will give the reader a sufficient key to the literature: *Arch. Exper. Path. u. Pharm.*, ii., viii., x. 125; xii. 77; *Zeitschr. f. Physiolog. Chem.*, ii. 29, iv. 36; *Zeitschr. f. Biol.*, xiv.

In failure of the heart during *anæsthesia*,* and in *poisoning* other than from snake-bite, hypodermic injections of ammonia† have seemed in a number of reported cases to be of very great service. The same may be said of *sudden collapse* in disease, as sometimes is seen in the *exanthemata*, in *cholera*, and not rarely in *pernicious malarial fever*,‡ or after *surgical operations* or *injuries*. From fifteen to twenty-five minims of the aqua ammoniæ fortior, diluted with four times its bulk of water, should be thrown directly into a vein of the arm, and repeated in fifteen minutes if necessary.

Prof. Stillé and other authorities claim for ammonia an antidotal influence in alcoholic intoxication; but that it can relieve absolute drunkenness is, I think, very doubtful. Ammonia appears to have a tendency to act upon the mucous membrane of the lungs, and may be used as a stimulant expectorant in adynamic pectoral inflammations, as in typhoid *pneumonia*. As a stimulant antacid, it is frequently of service in cases of *headache* from *gastric acidity*.

TOXICOLOGY.—When taken in large amounts, ammonia acts as a violent corrosive poison, producing generally abdominal pain, vomiting, bloody purging, and other symptoms of gastro-enteritis, with convulsions, collapse, and finally death. In some cases symptoms of impending suffocation, resulting in death from asphyxia, have occurred, and at the autopsy intense redness and congestion of the bronchial mucous membrane have been present, due no doubt to the irritant having found its way into the bronchi. The intellect may be clear to the very moment of death, or stupor, and finally coma, may be developed. In the rare instances in which death has taken place within five minutes from the ingestion of the poison, the fatal result has probably been brought about by œdema of the larynx. When the sufferer survives the first few hours, recovery may occur; but death sometimes happens long afterwards from the organic lesions which have been produced. The treatment of poisoning by ammonia consists in its neutralization as soon as possible by vinegar or other dilute acid, and the meeting of indications as they arise. If the œdema of the glottis be threatening, tracheotomy should at once be performed.

ADMINISTRATION.—There are four officinal preparations of uncombined ammonia itself,—namely, AQUA AMMONIÆ FORTIOR (*Stronger Water of Ammonia*), sp. gr. 0.900, AQUA AMMONIÆ (*Water of Ammonia*), sp. gr. 0.959, SPIRITUS AMMONIÆ (*Spirit of Ammonia*), and SPIRITUS AMMONIÆ AROMATICUS, or *Aromatic Spirit of Hartshorn* as it is usually called.

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* Prof. Sidney Ringer (*Practitioner*, xxvii.) finds that ammonia added to the frog heart depressed with chloroform, iodoform, etc., has a very pronounced effect in re-establishing its action.

† See *Indian Medical Gazette*, June 1, 1872; *Medical Times and Gazette*, Nov. 1872; *Chicago Medical Journal*, 1872; *London Medical Record*, i., 1873; *L'Abeille Médicale*, Aug. 1874; *Berlin. Klin. Wochenschrift*, No. 24, 1874; *Archives Générales*, ii., 1874; *London Lancet*, 1879, ii. 158; *New York Med. Rec.*, xv. 532.

‡ See Dr. Zuelzer, *Revue de Thérap.-Med.-Chirur.*, July 1, 1872.

To reduce the strength of the first of these preparations to that of the second requires the addition of one and a half measures of water. The spirit is of varying strength, but is somewhat weaker than the simple water. The aromatic spirit contains both ammonia and its carbonate. For hypodermic use the waters of ammonia are to be preferred. The spirits, especially the aromatic, are best suited for internal use. The dose of the simple spirit is from twenty-five drops to a teaspoonful, properly diluted.

The *Carbonate of Ammonium*, U. S. (AMMONII CARBONAS, $NH_4O,CO,$ $—2NH_4,$) is the best preparation for continuous use and in typhoid *pneumonia*. It occurs in white, translucent, fibrous masses, which on exposure become opaque and efflorescent, parting with ammonia and passing from a sesqui- into a bi-carbonate. It is soluble in four and a half times its weight of water, and may be given in solution in doses of from five to ten grains, repeated *pro re nata*.

The *Nitrate of Ammonium* (AMMONII NITRAS, $NH_4O,NO_5—NH_4NO_3$) is officinal for the preparation of nitrous oxide; the *Sulphate* (AMMONII SULPHAS, $NH_4O,SO_3—2NH_4,SO_4$), for the preparation of *Ammonio-ferric Alum*. The *Muriate of Ammonia* will be considered elsewhere.

ALCOHOL U.S.

Absolute alcohol, *i.e.*, alcohol free from water, is a colorless, volatile liquid, boiling at 172° F., not congealed by a cold of —166° F., and having the specific gravity of 0.796. It is not officinal, and is never used except for chemical purposes.

The U. S. Pharmacopœia recognizes ALCOHOL, containing 94 per cent. of absolute alcohol, and having the specific gravity of 0.820; ALCOHOL DILUTUM, *Dilute Alcohol*, containing 53 per cent. of alcohol, and having the specific gravity of 0.928.

Alcohol also exists in the officinal SPIRITUS FRUMENTI, or WHISKY, and SPIRITUS VINI GALLICI, or BRANDY, which are obtained respectively by the distillation of fermented grain and of fermented grapes, and should contain from 48 to 56 per cent. of absolute alcohol; and in the officinal VINUM RUBRUM, or *Red Wine*, and VINUM ALBUM, or *White Wine*.

For medicinal use, brandy should be at least four and whisky at least two years old.

Alcohol is formed out of sugar by fermentation; but, as a discussion of the natural history and chemistry of this process, to be of value, would occupy much space, the reader is referred for it to works especially devoted to chemistry and to materia medica.

PHYSIOLOGICAL ACTION.—The phenomena induced by the ingestion of alcohol are, unfortunately, so well known as to make any description of them here unnecessary. I have not met with a close experimental study of the order in which the nervous centres are affected, but it is scarcely doubtful that alcohol acts upon them as does ether, excepting that the latter substance, being much more volatile than the alcohol, is consequently absorbed and eliminated much more rapidly, so that its influence is more evanescent. I know by experiment that the vapor of alcohol is capable of producing the stupor known as anæsthesia, and, further, that this anæsthesia may be deepened into death, accompanied by all the phenomena of fatal ether-narcosis. The experiments of Mommsen (*Arch. f. Patholog. Anat.*, lxxxiii. 243) would seem to show that alcohol acts slightly upon the peripheral motor nerves, as he found that when brought into contact with them it augmented their excitability.

It is a well-known clinical fact that alcohol given to healthy men increases the frequency, and, to the fingers, the force of the pulse. The very careful and elaborate experiments of Parkes and Wollowicz upon man, with the sphygmograph, indicate that there is produced by brandy an increased rapidity of the ventricular contraction, with shortening of the period of rest or diastole. The tracings furnished, however, no distinct indications of increased arterial pressure. Dr. H. Zimmerberg found that enormous doses of alcohol reduce both the pulse-rate and force. After section of the vagi the alcohol lessened the arterial pressure without affecting the pulse-rate, whose slowing in the normal animal would therefore seem to be due to inhibitory stimulation. It is plain that Zimmerberg's experiments apply, not to therapeutic, but toxic, doses of alcohol. J. Dogiel affirms that by moderate amounts of alcohol the arterial pressure is at first increased and then diminished. During the latter state the vaso-motor centres are found incapable of responding to stimulation. The rate of the heart-beat is stated to be at first increased, then diminished, then increased; the first increase being owing to the stimulation of the accelerators, the diminution to stimulation of the par vagum, and the final increase to paralysis of the same. The action of alcohol upon the circulation has been carefully studied in the Pharmacological Laboratory of the University of Pennsylvania by Dr. J. D. Castillo (*Phila. Med. Times*, xi. 45). He found that in moderate doses the drug caused great increase in the rate and force of the cardiac beat and corresponding rise of the arterial pressure, and that these phenomena were not affected by previous division of the pneumogastrics, of the accelerators, or of the spinal cord. These results, so far as the pulse-rate is concerned, are in direct contradiction to those of Dogiel; but in regard to the arterial pressure they are partially in accord. On the other hand, closely corresponding with the results of Dogiel are the elaborate studies of Prof. Martin (*Maryland Med. Journ.*, x. 292) upon the dog's heart, isolated according to the manner invented by himself. Prof. Martin found that blood containing one-eighth per cent. by volume of absolute alcohol has no immediate action upon the isolated heart; that blood containing one-fourth per cent. diminishes within a minute the work done by the heart; blood containing one-half per cent. always diminishes remarkably the heart-work and sometimes nearly destroys it, so that not enough blood is pumped out of the left ventricle to supply the coronary artery. The curious observation was made that cutting away the pericardium stopped the action of even one-half per cent. of alcohol. The explanation of this offered by Prof. Martin is that the alcohol so relaxes the cardiac muscle that there is not room in the pericardium for a full diastole, the relaxed heart being, even in its systole, about sufficiently large to fill the pericardium. This explanation is hardly satisfactory. Can there be a local inhibitory cardiac apparatus, with peripheral filaments in the pericardium which are irritated by alcohol, and whose removal prevents the action of the alcohol? Whatever the explanation of Prof. Martin's results may be, it is clear that at present they do not warrant positive conclusions as to the action of alcohol upon the circulation. The experimental evidence is too fragmentary and contradictory to be put against the universal belief of clinicians, that *small doses of alcohol increase the force of the circulation by directly acting upon the heart.* Martin, Castillo, Dogiel, and Zimmerberg all agree that large doses of alcohol diminish very greatly arterial pressure. Castillo found that the lowering is produced after section of the cord, and that when it is very pronounced galvanic irritation of the sciatic causes a rise of pressure, showing that the vaso-motor centres are intact. This is in accord with the results of Martin, and it may be considered established that *overdoses of alcohol directly depress and paralyze the heart-muscle:* but it still seems probable that the fall of the pressure is also in part due to an influence exerted upon the arterial system.

Owing no doubt to the sensations of warmth induced by its local action on the stomach and by the increased activity of the circulation in the extremities, alcohol has been looked upon as a promoter of animal heat. As long ago as 1848, however, Duméril and Demarquay asserted that after the administration of large doses there is a fall of temperature. Of late years much attention has been given to the subject, and positive results have been achieved As almost all experimenters are in accord, it does not seem worth while to occupy space with a discussion of the history of the subject. References are given to the principal original memoirs.*

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* For those desirous of looking up the literature of the subject, the following references are given:

N. S. Davis, *Transactions American Medical Association,* 1855, p. 577. C. Bouvier, *Pflüger's Archiv für Physiologie,* p. 370, 1869; Obernier, *Ibid.,* p. 499, 1869. A. Godfrin, *De l'Alcool, son Action physiologique, ses Applications thérapeutiques,* Paris, 1869. C. Bouvier, *Wirkung der Alcohol auf die Körpertemperatur,* Bonn, 1869. Manassein, *Centralblatt für die Med. Wissenschaften,* 1869. P. Ruge, *Virchow's Archiv,* Bd. xlix. p. 265. C. Binz, *Virchow's Archiv,* Bd. li. p. 153; *London Practitioner,* vol. iii., 1869, vol. v., 1870; *Journal of Anatomy and Physiology,* vol. viii., 1874, p. 232; *Sitzungsberichte der niederrheinischen Gesellschaft für Natur- und Heilkunde, Mediz. Section,* July 21, 1873. Brown-Séquard, *Journal de la Physiologie,* 1859, p. 467. Jacobi, *Deutsches Klinik,* 1857. Tscheschichin, It is certainly demonstrated that lethal doses of alcohol produce in animals a fall of temperature which often amounts to 5° C., and that even when intoxication or alcoholic narcosis is alone induced the depression of temperature may amount to 3° C. The proportionate dose necessary to produce distinct nervous symptoms is enormous in the lower animals as compared with man; yet, after the ingestion of amounts of alcohol which are not enough to cause intoxication in the animal, the fall of temperature is slight,—rarely more than 1° C., and according to Ruge (*loc. cit.*, p. 265) usually from ⅙° to ⅚° C.

The experiments of Richardson show that in some cases very minute doses of alcohol increase slightly the temperature (½° F. in mammals, 1° F. in birds). As regards animal heat, alcohol acts upon man as upon the lower animals. After doses only sufficient to increase the activity of the circulation, probably as a result of this increase, there is sometimes a very trifling exaltation of temperature (Parkes and Wollowicz). After larger doses there is a slight fall of temperature, and when full intoxication is induced this fall may amount to 3° F. (Ringer and Rickards).

Upon animals suffering from pyæmic fever Bouvier and subsequent observers have found that alcohol exerts a decided antipyretic action, very large doses of it lowering the temperature as much as 8½° C., and altogether preventing the occurrence of fever if narcosis be produced before the development of the latter. In fever in man alcohol exerts a similar influence, but in order to make its antipyretic action decidedly manifest, doses so large as to be toxic must be given (Ringer and Rickards). It has been noticed both in man and in the lower animals (Bouvier) that when the individual is accustomed to the free habitual use of alcohol the temperature is scarcely affected even by large doses.

Very recently, Dr. Franz Riegel (*Deutsches Archiv für Klin. Medicin*, 1873) has made a very elaborate original investigation upon men, comprising as many as eighty-six experiments, and has arrived at the following conclusions, which are in exact accord with what was already in type when his memoir came to hand. As they embody the whole subject in a few words, and may be received as absolutely demonstrated, I offer no apology for interpolating them here:

"1. Alcohol, even in moderate doses, in many cases causes a lowering of the temperature of the body. The amount of this diminution averages as a rule

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Reichert's Archiv für Anatomie, 1866. Ringer and Rickards, *London Lancet*, 1866, p. 208. Richardson, *Medical Times and Gazette*, vol. ii. p. 704, 1869. Parkes and Wollowicz, *Transactions of the Royal Society*, 1870. Anstie, *Stimulants and Narcotics*, London. Mainzer, *Ueber die Wirkung des Alkohols auf die Temperatur des Gesunden*, Inaugural Dissertation, abstracted by Binz in *Virchow's Archiv*, Sept. 1871. C. Bouvier, *Centralblatt für die Med. Wissenschaften*, Dec. 1871. I. S. Lombard, *New York Medical Journal*, June, 1865. Sulzynski, *Ueber die des Alkohols, Chloroforms und Ethers Einfluss auf den thierischen Organismus*, Inaugural Dissertation, Dorpat, 1865. S. Rabou, *Berlin. Klinische Wochenschrift*, 1871. Radziejewski, *Centralblatt für die Med. Wissenschaften*, 1871. Gustav Strassburg (use in fever), *Virchow's Archiv*, Bd. lx. p. 471. L. Lewin, *Centralblatt für die Med. Wissenschaften*, No. 38, 1874.

only some tenths of one degree. 2. Only exceptionally is there noticed an elevation of the temperature consequent upon the administration of alcohol; not unfrequently, at least after minute doses, there is no noticeable change. 3. The diminution of temperature in convalescents is, as a rule, less than in healthy subjects, or it may be altogether wanting. 4. In those who habitually drink alcoholic stimulants, the depressing influence of alcohol upon the temperature is almost always wanting. 5. The frequent repetition of the doses of alcohol diminishes their lowering effect upon the temperature. 6. The amount of diminution of temperature is directly proportional to the dose of alcohol given. 7. The depression of temperature caused by alcohol is for the most part of but short duration, and the temperature soon returns to its previous grade."

The effect of alcohol upon the formation of animal heat was first properly studied by Dr. Bevan Lewis (*Journal of Mental Sci.*, xxvi. 20). He found that after the exhibition of alcohol in the rabbit there was sometimes a primary lessening of heat production of very short duration, which was followed by a marked increase in the heat production. In some cases heat dissipation more than kept pace with this increase and the bodily temperature fell; in other instances the bodily temperature rose, showing that heat production was excited more than heat dissipation. Calorimetrical experiments made by myself and Dr. Reichert have arrived at similar results, but before it can be shown exactly how alcohol affects thermogenesis further experimentation is needed. It may be that the increased heat generation is simply the result of the rapid burning up of the alcohol itself. The great fall of bodily temperature which occurs after toxic doses of the drug seems to me to be clearly due to excessive heat dissipation, which in turn is the result of vaso-motor paralysis.*

The effect of alcohol upon the elimination of carbonic acid by the lungs has been investigated by several observers, with different results. According to the researches of Böcker (*Beiträge zur Heilkunde insbesondere zur Krankheitsgenussmittel und Arzneiwirkungs Lehre*, abstracted by Claude Bernard in *Journal de Pharmacie*, tom. xv., 3d series, 1849), of N. S. Davis (*Transactions of the American Medical Association*, 1855), of Hammond (*Physiological Memoirs*, Philadelphia, 1863), and of M. Perrin (*Archives Générales*, 6th series, tome iv.), there is a decided lessening in the amount of carbonic acid gas exhaled. Dr. E. Smith, however, found that small doses of alcohol increased the elimination of the gas, although brandy, whisky, and gin always lessened the production. It is probable that the action of the small doses of spirits taken may vary, as it is readily conceivable that by checking or aiding digestion, by influencing the circulation, or in some other way, they may at times exert an indirect action which shall overcome any direct influence they may possess. Be this as it may, the weight of evidence appears to be at present in favor of their usually diminishing the elimination of carbonic acid; although the matter cannot be considered as entirely settled.

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* Prof. Binz's experiments and inferences upon this subject, in the light of recent evidence, seem of no value.

One of the most important facts to be determined about alcohol is its influence upon the excretion of nitrogenous material. Böcker is commonly believed to have experimentally determined that it lessens the excretion of urea. I have seen only an abstract of the original paper. In it this is not positively asserted, but seems to be inferred. Dr. Hammond has performed a very elaborate series of experiments upon himself: first, when just sufficient food was taken to maintain the weight of the body; second, when more than enough for that purpose was ingested; third, when not enough was taken. Under all these circumstances, urea, chlorine, and phosphoric acid were lessened in amount by the ingestion of alcohol. Parkes and Wollowicz (*loc. cit.*) affirm that their experiments gave a contrary result. In examining the reports of their experiments I find, however, that on one of the days the man taking the alcohol had a chill followed by fever. If this day be omitted, the average daily excretion of urea during the alcoholic period was 34.35 grammes; during the time when brandy was taken, 34.8 grammes; and during the water period, 35.02 grammes. The ingestion of alcohol seems, therefore, to have reduced the elimination of urea by about ten grains a day. Recently very careful experiments have been made by L. L. Rieso (*Hoffmann und Schwalbe's Jahresb.*, 1881, 357) upon two persons under rigid conditions. The exhibition of alcohol was followed by great lessening of the excretion of urea, and to a less pronounced degree of uric acid, chlorides, phosphates, and sulphates, and at the same time an increase of the bodily weight. These results are in strict accord with those of Hammond, and it must be considered fairly proven that alcohol causes *a great lessening in the excretion of the products of tissue waste.*

From the time of Liebig's celebrated classification of food until the appearance of the memoir of MM. Lallemand, Duroy, and Perrin, ingested alcohol was almost universally believed to be burnt up in the body. These latter observers asserted, however, that alcohol escapes unchanged from the body, not only because they were unable to detect in the blood or tissues any of the results of its oxidation, such as aldehyde or acetic acid, but also because they found it unchanged in the expired air, the sweat, and especially in the urine. The results obtained by the French investigators were, however, seriously questioned by E. Baudot (*L' Union Médicale*, 1863), who demonstrated that the chromic acid test which Duroy and Perrin had relied on for detecting alcohol in the excretions is so delicate as to reveal .165 grain of alcohol in a quart of water; and Baudot further affirmed as the result of twenty experiments that except after immense doses the amount of alcohol eliminated by the kidneys is so small as practically to amount to nothing. In 1866 Dr. Schulinus (*Archiv der Heilkunde*, 1866), by a very elaborate and laborious investigation, confirmed the results of Baudot, showing that alcohol taken into the blood finds its way by exosmose into all organs in similar proportion, and does not escape through the kidneys unless in very trifling amounts. In several experiments he found that one-fourth of the ingested alcohol had disappeared from the body after from two to three and one-fourth hours, and, as but a fractional portion of the lost amount was eliminated, he concluded that it must have been burnt up. Adolph Lieben (*Annalen der Chemie und Pharmacie*, 1870, vii., Supplement. Bd. p. 236) has in a number of experiments arrived at results similar to those of Schulinus.

In 1865 a number of experiments yielded to Anstie, of London (*Stimulants and Narcotics* (reprint), Philadelphia, 1868), similar results, and also demonstrated that the elimination from the lungs is exceedingly trifling. Thudichum investigated the matter on a large scale in 1864, and again with the assistance of Dupré in 1866 (*Tenth Report of the Medical Officer of the Privy Council*, London, 1868). In order to avoid the fallacies of the chromic acid test, the alcohol was obtained from the urine by repeated distillations. In the first instance forty-four bottles of wine, containing four thousand grammes of alcohol, were drunk by thirty-three men, out of whose urine, collected during the next six hours, ten grammes, or only 0.25 per cent., of the ingested alcohol were recovered. In the experiments of 1866 the process was substantially the same, but, greater care being taken to get absolute accuracy and to avoid loss during distillation, 0.82 per cent. of the amount administered was found in the urine. Quite recently, Subbotin (*Zeitschrift für Biologie*, vii., 1871; *Schmidt's Jahrbücher*, 1872, Bd. cliv. p. 261) has made an apparently close experimental study of the subject upon six rabbits, and has shown that elimination continues for a longer time than had been generally believed, and that twice as much of the alcohol escapes by the skin and lungs as by the kidneys. In one experiment he found that 16 per cent. of the alcohol escaped unchanged in the first twenty-four hours; elimination after this time, although perceptible, amounted to very little. As he, like Lallemand and his colleagues, experimented with poisonous doses, his results confirm rather than contradict those of Baudot, Schulinus, Anstie, Thudichum, and Dupré; for it is manifestly evident that after such doses elimination would be proportionately greater than after smaller quantities, as there naturally must be a limit to the powers of the system to oxidize alcohol. Prof. R. D. Edes, in his experiments (*Boston Medical and Surgical Journal*, 1872, p. 347), found that after small doses the amount of elimination by the breath is greater than that by the kidneys, although the contrary holds where large amounts have been administered: in either case the total amount eliminated was but a small percentage of that ingested.* Finally, Anstie

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* Prof. Edes relied upon the chromic acid test, which Binz asserts to be fallacious. In the experiments made by Stenbach and Schmidt, under Prof. Binz's direction, alcohol could not be detected in the breath, and Prof. Binz believes that no elimination of it occurs from the lungs. He declares that the odor of the breath after drinking is not that of alcohol, but of the ethers and other volatile principles of the various liquids imbibed.

(*London Practitioner*, July, 1874) has recently repeated his experiments, using the method of Subbotin, and even subjecting a dog, which had been taking for some days very much larger amounts of alcohol than he had eliminated by skin, kidneys, rectum, and lungs, to distillation, with the results of confirming his first experiments and of finding no "residual alcohol"—*i.e.*, alcohol left in the body—worthy of mention. In an elaborate research, Dr. Guido Bodländer found that he himself, after the use of alcohol in various quantities, eliminated by the kidneys about 1.2 per cent., and by the lungs about 1.6 per cent.; whilst in dogs he recovered from the breath about 2 per cent., from the urine 1.6 per cent., from the skin 0.14 per cent. of the ingested alcohol. He failed entirely to find alcohol in the intestinal excretions, and also, contrary to Lewald's observation in 1857, in the milk of a goat, to which nearly a quart of brandy had been given (*Archiv f. Physiolog.*, xxiii.).

These concurrent investigations* certainly demonstrate that but a small proportion of ingested alcohol is either eliminated from or accumulated in the body, and consequently that it must be oxidized in the body, and in some degrees partake of the nature of a food. It has been objected to this that no one has as yet been able to detect† in the blood any of the ordinary products of its oxidation; the probable reason of this is, however, that the oxidation is carried as it were at one bound to its ultimate end, the production of water and of carbonic acid. A strong corroborative proof that alcohol is largely consumed in the body is furnished even by the experiments of Lallemand, Duroy, and Perrin themselves, for they proved that elimination ceased, or at least could not be detected by the most delicate tests, *before* the alcohol had all escaped from the body.

A very strong confirmation of the theory that asserts the oxidation of alcohol in the body is found in the researches of our countryman Dr. H. Ford, whose experiments have, however, not been repeated, and therefore, although apparently carefully performed, lack the absolute authority of complete confirmation. Dr. Ford (*N. Y. Med. Journ.*, Jan. 1872) has worked upon the supposition that the hepatic sugar must be converted into alcohol in the body before its final destruction, and, using large quantities of blood of animals, has sought by repeated distillations to obtain alcohol from it.‡

Pushing his researches still further, Dr. Ford used various tissues as the substances to be distilled. He also made elaborate calculations, based on the carbon ingested and on the carbon exhaled, as to the amount of alcohol which ought to be found in the capillary blood of the lungs. The results are expressed in the following table:

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* I believe these results have also been confirmed by Wöhler, *Journal des Progrès*, xi., but I have not seen the original paper or any abstract of it.

† Duchek (*Vierteljahr. Prakt. Heilk.*, Bd. iii., 1853) did not, as he thought, demonstrate the presence of aldehyde in the blood of animals poisoned with alcohol.

‡ Space is wanting to describe in detail the very elaborate methods employed by Dr. Ford. The tests which he relied on, to prove that the liquid obtained was alcohol, were the chromic acid test, the peculiar inflammability, and the optical appearance of the alcohol in the conducting-tubes at the time the distillate commenced to boil. In order to prevent any possible oxidation of the alcohol during the process, Dr. Ford sometimes added

Alcohol in the capillary blood of the lungs:

	calculation based on "*carbon ingested*" . .	0.5403
	" " " "*carbon exhaled*" . .	0.5794
"	putrescent lung-tissue (mean of exp. 8, 9, and 11). .	0.3819
"	fresh " (" " 12, 13, and 14). .	0.3076
"	putrescent thoracic blood (mean of exp. 1, 2, 3, 4, and 5) .	0.7625
"	fresh " " (mean of table)	0.0841
"	putrescent liver-tissue (exp. 6)	4.3138
"	fresh " (mean of exp. 25, 26, and 27) .	0.0190

The important facts seemingly established in the above table are: the correspondence between the amount of alcohol in the thoracic blood as obtained by calculation and by experiment; that the smallest quantity of alcohol is to be obtained from fresh liver-tissue, the greatest from putrescent liver-tissue, in which the glycogen must have undergone fermentation. The fresh thoracic blood was blood which had not traversed the lungs; the putrescent thoracic blood of course represented the same blood with all its sugar fermented.

These researches of Dr. Ford are certainly corroborated by the discovery, first made, I believe, by A. Lieben (*Annalen der Chem. und Pharm.*, 1870), although usually attributed to Dupré (*The Doctor*, Feb. 1, 1873), that a substance exactly resembling alcohol exists in very minute quantity in the urine even of teetotalers.* M. Béchamp (*London Lancet*, 1873), apparently without a knowledge of the work of the other chemists, obtained, from the urine of persons who had not taken any alcoholic beverage for a long time, alcohol in sufficient quantity to burn it. As Lieben also found that this sub-

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sulphuretted hydrogen. The results of ten experiments are shown in the following table:

No.	Weight of Blood.	Interval from Death to 212°.	Temperature when distilled.	Weight of First Distillation.	Weight of Final Distillate.	Weight of Alcohol obtained.	Weight of Alcohol for 10,000 parts of Blood.	With or without HS.
15	6970	60 m.	....	....	....	0.0650	0.0932	without.
16	9734	56	101°	1602	0.8416	0.0198	0.0203	without.
17	9137	70	100.3	1636	1.6218	0.0605	0.0662	with.
18	9236	77	99.5	1623	3.6130	0.0444	0.0480	with.
19	8988	60	99	1555	2.6092	0.1357	0.1509	with.
20	8854	60	98	1555	1.7320	0.0760	0.0858	with.
21	9423	45	96	1560	1.8722	0.0708	0.0751	without.
22	9112	61	98	1550	0.9552	0.0350	0.0384	without.
23	27330	48	98	14050	10.6883	0.2928	0.1071	with.
24	36300	51	99	17600	14.0606	0.5652	0.1556	with.

* It is asserted that the substance "is not alcohol. It passes over among the earliest products of distillation, yields acetic acid on being oxidized, reduces the bichromate of potassium when dilute sulphuric acid is present, and its aqueous solution has a lower density than water. It furnishes iodoform, and exists in the urine in a very small quantity." Possessing the physical and chemical characters of alcohol, to ordinary minds it is alcohol.

stance exists in the urine of dogs, horses, and lions, and A. Rajewski obtained it from healthy rabbits (*Archiv für Physiologie*, xi. p. 122, 1875), its existence in the normal organism must be considered demonstrated.

Upon the nervous system alcohol exerts a powerful influence. Its effects upon the cerebrum are too well known to require elaboration; but it may be mentioned that I. Dogiel (*loc. cit.*) has found that in frogs the reflex susceptibility is at first somewhat, and afterwards decidedly, diminished by large doses of alcohol, and that the sensory and motor nerves are similarly affected.

The question of the effect of alcohol upon digestion is an important one. There can be no doubt that very large doses hinder digestion. According to the experiments of W. Buchner (*Deutsch. Arch. f. Klin. Med.*, xxix. 537), ten per cent. of pure alcohol does not affect artificial digestion, whilst beer, even diluted, retards it. The use even of small doses of alcohol seemed to delay digestion in a few experiments made by washing out the stomach a fixed time after a meal taken sometimes with, sometimes without, alcoholic drink. The method is, however, too crude to allow much weight to the experiments; for it is possible that alcohol may lessen the rapidity with which the food leaves the stomach, and therefore aid in the thoroughness of gastric digestion. Certainly every-day experience teaches us that in small amounts wines and liquors enable the *bon vivant* to digest more than is natural or proper.

From what has been said, it is certainly deducible that alcohol in small amount is an *arterial* and *cerebral stimulant*, increasing functional activity in the nervous and circulatory apparatus; is a *food*, in the sense that it is destroyed in the system and yields force which is utilized by the organism; is, when in sufficient quantity, a retarder of tissue changes, checking the excretion of nitrogen.

If alcohol be oxidized in the body, and be a food, as it seems to me is clearly proven, it must of course generate force, measurable by the modern standard of the heat-unit. A little calculation will show the importance, or rather the great amount, of the generated force. According to Dupré (*London Practitioner*, vol. ix., 1872, p. 33), one gramme of alcohol oxidized in the body evolves 7184 units of heat, whilst the same weight of lean beef gives off only 1482 units of heat. It has been estimated that 9.3 ounces of lean beef —equal to about two ounces of alcohol—will supply the necessary force to maintain the circulation and respiration of an average man for one day. That is, four ounces of strong spirit will suffice for this purpose. Since to the ability of furnishing material whose consumption shall give power is added the ability to restrict waste and to stimulate the functions of circulation and of the nervous system, it is evident that in alcohol we have a most important means of sustaining the system during the strain of an acute exhausting disease.

THERAPEUTICS.—Our knowledge of the physiological properties of alcohol shows that its chief therapeutic value in acute disease is as a stimulant, a temporary imparter of power which shall enable the system to stand some strain of like duration,—to bridge over some period of weakness.

The cases to which it is especially adapted may be divided into three classes.

First. Those in which there is a temporary loss of heart-power, as in fainting from exhaustion, loss of blood, or other cause. In these cases the alcoholic stimulant should, if possible, be given hot, and not much diluted; with it should also be exhibited some more rapidly-acting diffusible stimulant, such as ammonia.

Second. Those acute diseases in which the powers of the system are in danger of being used up; to aid in the digestion of food and in the maintenance of power. Alcohol, as has already been stated, is to a certain extent a food, but it will not of itself sustain life for a long time, and should in adynamic disease always, unless for special reasons, be combined with milk, or occasionally with eggs. One great source of its value in these diseases is the power it imparts of assimilating food, and in milk-punch are furnished the stimulant to digestion and the most perfect food known for digestion. This use of alcohol is apart from its office in the lowest stage of fever as a heart- and nerve-stimulant. Employed for this purpose it is useful in *all* stages of the *adynamic fevers*, such as *typhus* and *typhoid.* By the exhibition of three or four ounces of milk every two hours, with one or two drachms of brandy or whisky, from the beginning of the attack, in many cases the development of the severe adynamic symptoms may be prevented.

In the advanced stages of diseases, when the *typhoid state* is well developed, alcohol should be given boldly,—to quiet by stimulation the nervous and circulatory systems,—to afford a food which shall in a measure replace the natural pabulum,—to aid in the digestion of milk and other simple nourishment,—to aid in lowering temperature by checking the tissue-waste of fever: in a word, to enable the system to stand the drain upon its vital powers, and at the same time to check such drain.

Properly administered, it always promotes, not arrests, secretion in these cases. The guide to the amount given should be the effects produced: so long as it lowers temperature and pulse-rate, moistens the dry tongue and skin, and quiets the nervous disturbance, it does good; if, however, the tongue grows drier, the pulse puts on an angry, bounding character, and the patient becomes restless and uneasy, stimulation is being pushed too far, and the amount exhibited should be lessened. The antipyretic action of alcohol has suggested its use in all cases of high temperature; as, however, this is only one of its actions, and as it is not decided unless very large doses be given, alcohol cannot be employed as a general febrifuge. True arterial excitement and sthenic inflammation certainly contra-indicate its use. The rule may be laid down as follows: high temperature is an indication for the use of alcohol only when other symptoms also demand it; in itself high temperature is never a contra-indication to alcohol. In *acute sthenic diseases*, after the progressive stage has passed and the results of the disease simply remain to be overcome, alcohol and milk will often save life. Thus, in *acute pneumonia*, when so much consolidation has occurred as to render it doubtful whether the exuded matter can be removed, or in *abscess*, when large amounts of pus have formed, the demand may be very great for alcohol as a food and as an aider of digestion, and sometimes as a stimulant.

Third. Those in which there is a depressing agent. In many forms of *poisoning*, alcohol may be used with signal advantage simply as an arterial and nervous stimulant, to overcome the influence of a depressing agent. Thus, in *snake-bite* the unlimited use of it affords, with the hypodermic use of ammonia (see Ammonia), the best method of treatment. Recently it has been very strongly recommended in *pyæmia* by Dr. Theodor Clemens, of Frankfort (*Deutsche Klinik*, 1874, 1875), who states that he has seen eight cases of a severe type recover under the administration of red wine in as large amounts as the patient would drink. In *poisoning* by *aconite*, *veratrum viride*, or other similar substance, where death is threatened through failure of the heart-power, alcohol in some form is imperatively needed. In all these cases of acute depression threatening a fatal issue, it should be administered freely, not much diluted, and, if convenient, hot. From one to four ounces of whisky should be given, repeated every ten or fifteen minutes, until slight intoxication, convalescence, or death has resulted.

What has been said up to this point in regard to the therapeutic action of alcohol has had reference to acute disease. The value of the drug in some chronic diseases cannot be doubted; but in prescribing it the physician should never lose sight of the possible danger of producing a habit far worse in its fruits than death itself.

In *chronic neuralgia*, in *hypochondriasis*, in *melancholia*, temporary relief may sometimes be obtained by the use of stimulants; but the very relief afforded doubles the temptation to the frequent use of the alcohol, and, as the system becomes habituated to its action and the dose has to be more and more increased, the habit of frequent stimulation grows almost of necessity into drunkenness. For this reason I do not think the physician is ever justified in prescribing alcohol for its narcotic stimulant effect in these cases. The chief legitimate uses of alcohol in chronic diseases are to aid in digestion; to furnish a food which, without any digestive effort upon the part of the system, shall be absorbed and shall take the place of more ordinary food; and to check excessive tissue-waste. Of course these indications exist only in such diseases as are either dependent upon or closely associated with a condition of system in which the general nutrition is depraved. In purely local affections the use of alcohol is rarely called for except in the last moments of life, when it may always be employed to afford relief and to protract for a short time the struggle. In *chronic dyspepsia*, alcohol administered with the food often aids very materially in the assimilation of the latter; but care has to be exercised in prescribing it, for the same reasons as were given when speaking of the use of stimulants in melancholia a moment since. In many cases of *chronic neuralgia*, not as a narcotic stimulant, but as a food and a stimulant to nutrition, alcohol is often of the greatest service. The danger of establishing a fatal habit in this disease is, however, excessive. In almost all cases in which alcohol is called for in neuralgia, cod-liver oil is also indicated, and it is generally best to exhibit the two remedies together, so as to obtain the easy assimilation of the oil and to guard against evil moral results.

In *phthisis* and its congener *scrofulosis*, there can be no doubt as to the great value of alcohol; and in the latter stages of consumption its judicious use as an antipyretic narcotic stimulant to lessen the sufferings of the patient is perfectly justifiable. During the chronic movements of the affection, alcohol taken with cod-liver oil, or in small amounts with the food at meal-times, conduces not so much to the comfort as to the well-being and recovery of the patient.

The question as to the propriety of the daily use of alcohol by healthy men is at present a very serious one, involving so many moral and politico-moral issues that it cannot be fully discussed here. Suffice it to state, as obvious inferences from our present knowledge of the physiological action of alcohol, that the habitual use of moderate amounts of alcohol does no harm; that to a certain extent it is capable of replacing ordinary food, so that if the latter be scanty, or even if it be coarse and not easily digested, alcohol, in some form or other, is of great advantage; that in all cases it should be taken well diluted, so as not to irritate the stomach; and that wine or malt liquors are certainly preferable to spirits. The experience of Arctic explorers has certainly shown that alcohol has no heat-producing power, so that at a time when it was believed to have such influence by physiologists the Northern navigators had learned that the free use of spirits, far from enabling a man to withstand habitual exposure to intense cold, very materially lessened his power of resistance. On the other hand, the experience of almost every trout-fisherman or sportsman has satisfied him that spirits do have power to prevent "catching cold" under sudden and unaccustomed exposure to wet and cold, and that benumbed extremities will become warm and have their proper feelings return under the influence of a glass of whisky. There is, however, nothing strange or contradictory in these experiences, and they are both in strict accord with the present knowledge of the physiological action of the drug. As is often the case, the facts were practically made out, however, before science could solve the apparent paradox. As has been abundantly shown, alcohol has no heating power; but the chill of sudden exposure, the suffering benumbed extremities, the bronchitis that perhaps follows, all mean simply this: that, as the result of the cold, the blood leaves the surface and the extremities, the circulation fails in the outposts, and, as a consequence, suppressed perspiration—*i.e.*, suspended function of the skin—and internal congestions result. The relief afforded by the spirits, as well as the prevention of sickness, is due simply to the power of the remedy in maintaining the circulation and keeping the external surfaces warmed by the constantly-renewed currents of fresh blood from the interior of the body.

Owing to its stimulant and antiseptic properties, alcohol constitutes an excellent dressing for wounds, whether accidental or surgical in their origin. It would seem also to lessen pain by a local anæsthetic effect (Horvalle, *Gaz. des Hôpitaux*, Sept. 1878). Strong surgical testimony as to the local value of whisky has been given by Drs. Blair (*Glasgow Med. Jour.*, Feb. 1870) and Suesserott (*Phila. Med. Times*, vol. iv. p. 774). Lint soaked and kept constantly wet with spirits is to be packed on or in the wound.

ADMINISTRATION.—Almost enough has been already said upon this point, but a few further remarks seem appropriate. When stimulants are used to sustain the sinking powers in poisoning or in disease, the amount given should be almost solely regulated by the effects. Thus, in snake-bite it may be necessary to give a pint of whisky in the course of an hour; and in low fevers I have seen the greatest benefit result, and life apparently saved, by the exhibition of a quart of spirits a day. The rule is always to be governed by the effects. In poisoning, one, two, three, or four ounces, as the case may seem to need, should be exhibited every ten minutes, until some effect is produced or matters become hopeless. In low fevers half an ounce to an ounce should be given every one, two, or three hours, *pro re nata*, the practitioner watching the results, as already spoken of.

The question of choice, of course, comes up in every case as to which of the spirits shall be used. I have never been able to perceive any difference in their action (gin, of course, being excepted), save only that sometimes one agrees better with the stomach than the other. This has seemed to me to depend simply upon the personal likings of the patient, to which therefore the choice may well be left. In sudden collapse, some of the wines with a very high *bouquet* are believed to be more stimulating, on account of the ethers which they contain; but I have had no experience with them. In convalescence, and for habitual use in health, wines are preferable to spirits,—more agreeable, more tonic, and less apt to lead to excessive indulgence.

When a mild stimulant is wanted in the beginning of fevers, especially if milk-punch seems too "heavy," *wine whey* may be sometimes used with advantage. It is made by pouring a half-pint of sherry or madeira into a pint of boiling milk, stirring thoroughly, and after coagulation has occurred straining off the whey, which may or may not be sweetened, according to the taste of the patient. *Mulled wine* is often very grateful to patients as a change. It is made by beating an egg up thoroughly with three fluidounces of sherry and adding a like quantity of water, which must be actually boiling when poured in. *Champagne* is useful in patients with delicate stomachs, especially if nausea or vomiting actually exists, and also may be employed with advantage in sudden failure of the vital powers, especially in elderly persons. It must always be very "dry," *i.e.*, as free as possible from sugar.

Milk-punch is prepared by adding from a dessertspoonful to a fluidounce of brandy, whisky, or rum, according to the degree of stimulation required and the taste of the patient, to three fluidounces of milk, with sugar and nutmeg to taste. The addition of a tablespoonful of lime-water is not recognized by the palate, and renders the beverage more acceptable to the stomach when the latter is weak.

Egg-nogg is still more nutritious than milk-punch, but is "heavier," and is usually rejected by the stomach if given too freely. It is made by beating up thoroughly the yelk of an egg with five fluidounces of milk and half a fluidounce to one fluidounce of spirits (and half a fluidounce of lime-water if required), and adding a sufficiency of sugar, with finally the white of the egg previously thoroughly beaten into a froth.

TOXICOLOGY.—The acute form of alcoholic poisoning in its minor degrees is, unfortunately, an hourly occurrence almost in every village, but that fatal results are not absolutely so rare as is generally believed is shown by the fact mentioned by Taylor, that in four years (1863–67) thirty-five deaths from this source occurred in England and Wales. It is worthy of note that in some fatal cases convulsions have preceded death (*Phila. Med. Times*, vi. p. 463). The absolute diagnosis of acute alcoholic poisoning when the patient is simply seen in the advanced stage of deep coma cannot be made out. The odor of liquor upon the breath or about the person is simply a proof that the subject has been drinking, not that the symptoms are caused by alcohol. The manifestations are merely those of profound compression or congestion of the brain, of apoplexy, of opium-poisoning; and a man who has been drinking only moderately may have been struck down with apoplexy or poisoned with opium. Dr. Hughlings Jackson has recorded a case in which the alcohol impregnated not only the breath but the urine also, and in which the patient was left to sleep it off; but at the post-mortem a clot was found covering nearly the whole of one hemisphere. After death in acute alcoholic poisoning the stomach is found very much congested, and sometimes ecchymosed. The treatment consists in the evacuation of the stomach, the use of the alternate hot and cold douche, and the usual mechanical methods of arousing a narcotized patient.

TEREBINTHINA.—TURPENTINE. U.S.

White Turpentine is the concrete oleoresin obtained by incising the Pinus palustris and other species of pine. The supply in the American market comes almost exclusively from North Carolina and other of our Southern States. It is rarely, if ever, itself used in medicine, but by distillation is separated into a volatile oil and a resin (*Rosin*), which is officinal under the name of *Resina*. Rosin is used in medicine solely in the formation of certain plasters, chief among which is the *Emplastrum Resinæ*, U.S., *Adhesive Plaster*, or, in ordinary language, "*Sticking Plaster*," which is formed by adding rosin to lead plaster.

OLEUM TEREBINTHINÆ—OIL OF TURPENTINE. U. S.

This is a yellowish, highly-inflammable oil, of a strong peculiar odor and a hot biting taste, moderately soluble in alcohol, freely so in ether, very slightly so in water. By heating with muriatic acid it is converted into a red liquid and a white crystalline substance, which, from its resemblance to camphor, has received the name of *artificial camphor*. Turpentine is remarkable for having the property of absorbing oxygen and converting it into ozone.

Physiological Action.—Turpentine is a powerful irritant, causing in a very short time inflammation in any tissue with which it comes in contact.

When taken by a healthy person in moderate doses, it produces a sense of warmth in the stomach, soon followed by exhilaration, and, if the amount be sufficient, giddiness and even a species of intoxication. The pulse is increased in force and frequency. The turpentine escapes from the body through the lungs and kidneys, imparting its own odor to the breath, and that of violets to the urine. Although several recorded instances prove that turpentine is capable of producing death, yet cases of serious poisoning by it are rare, and a lethal result exceedingly so. The symptoms noted in poisoning by it are most of them constant, but vomiting and purging are present in some cases and not in others. Unconsciousness is generally complete, and in some cases is accompanied by dilated pupils; the urine is very much lessened in quantity, often bloody, not rarely suppressed; the skin is sometimes dry, sometimes moist; the pulse is feeble, rapid, and generally regular. The intense irritation of the urino-genital organs in some cases has been indicated by constant priapism and efforts at micturition.

The lethal dose must be very large, but is not definitely known, since recovery from four ounces in an infant fourteen months old has been reported. In Dr. Maund's case (*Annuaire de Thérapeutique*, 1846), death was supposed to have been produced in an intemperate woman by six ounces; and Philip Miall has recorded an instance of death produced in an infant fourteen weeks old by turpentine, of which half an ounce was thought to have been taken (*London Lancet*, March, 1869).

Turpentine appears to be a stimulant to the circulation and to some of the nerve-centres, but further study of its exact influence is still needed. R. Kobert (*Centralbl. für Med. Wissens.*, 1877, p. 129) found that in moderate doses it exerted a powerful stimulating influence upon the inhibitory reflex centre, and also elevated the blood-pressure by stimulating the vasomotor centre. Very large doses appeared to paralyze both of the centres spoken of, causing decided fall in the arterial pressure. The respiration was first increased in frequency, but later strongly diminished. The blood became very dark and the heart was finally paralyzed. The vagi and depressor nerves did not appear to be affected, nor did indeed any of the peripheral nerves, or the muscle. It is said that these results are in accord with those previously published by Azary in the Hungarian language. F. Fleischmann (*Schmidt's Jahrb.*, Bd. clxxx. 125) found that two drops produced paralysis in the frog—first of voluntary, and afterwards of reflex activity; in the cat and rabbit, toxic doses abolished reflex activity, but caused violent lethal convulsions. Dr. Hoppe (*Journal für Pharmacodynamik*, Bd. i. p. 105) concludes that the vaso-motor nerves are the first to feel the influence of the drug.

Upon the kidneys turpentine acts decidedly, causing, according to the size of the dose, increased secretion, or symptoms of renal irritation, such as pain in the back, and strangury, with a diminished excretion of bloody urine. Leon Crucis (*De la Térébinthine*, Paris Thesis, 1874) has made some experiments which indicate that when turpentine is given in toxic doses to rabbits it increases the coagulability of the blood and gives rise to numerous minute hepatic and pulmonic thrombi.

THERAPEUTICS.—Externally the oil of turpentine is very much employed as a powerful counter-irritant. It is useful more especially when it is desired to act upon a large extent of surface. When a very intense permanent local impression is required, a blister is to be preferred. Thus, in *pleurisy* a blister may be used, in *bronchitis*, turpentine stupes. In preparing the latter the turpentine should first be warmed by setting the vessel containing it in hot water, then a piece of flannel, just previously saturated with hot water and wrung as dry as possible, should be dipped in the turpentine and again wrung out. It is then ready for application, and may be left on from fifteen minutes to half an hour, according to the sensitiveness of the skin.

Another local use of the oil of turpentine is as an addition to enemata. From a teaspoonful to an ounce of it mixed with double its amount of olive oil renders opening enemata much more active, especially in causing the expulsion of flatus. Turpentine enemata containing much of the oil in a small bulk are also constantly used with good effect in arousing the system from stupor arising from narcotic poison or similar causes.

In *ulceration of the bowels*, turpentine taken by the stomach is often very efficient, probably acting locally in the intestine, and in *simple gastric ulcer* the very best results are sometimes derived from its use. In a single large dose (f℥ss to f℥i with an equal amount of castor oil) it is a very efficient vermifuge, especially against the round-worm. It also may be used as a stimulant in *low fevers*, particularly when the tongue is dry and red.

In *typhoid* or *enteric fever* it without doubt acts as a local stimulant to the ulcerated bowel, besides influencing the general condition of the system. There are two conditions or stages in the diseases named in which it is especially useful,—indeed, is of incalculable service. About the end of the second week the tongue sometimes becomes very dry, red, chapped, perhaps coated in the centre with a brownish fur, and at the same time marked meteorism develops. Ten drops of turpentine every two hours during the day and every three hours during the night will in the majority of cases remove the bad symptoms noted. That the action of the oil is largely a local one is shown not only by the arguments of the introducer of the practice, Dr. George B. Wood, but also by the value of the same treatment when diarrhœa persists after the acute stage of the fever has passed. When convalescence is protracted, when there is a constant tendency to the recurrence of diarrhœa, when, in other words, the ulcers of Peyer's patches are slow to heal, turpentine acts almost as a specific.

In *typhoid bronchitis* and *pneumonia*, especially as intercurrent in typhus fever and similar diseases, turpentine applied externally and taken internally is often very useful. The same may be said of the low forms of *puerperal fever*. In this disease the abdomen should be kept covered with fomentations of the oil and of warm water alternately, the counter-irritant being used as constantly as a proper regard for the skin of the patient will allow. Internally it should be given in very large doses (f℥ss) every two hours.

In *hemorrhages* from the stomach, bowels, or lungs, turpentine has acquired celebrity, but is hardly so much used as formerly. It is in the ataxic cases that it is useful. I have very rarely employed it, as the *oil of erigeron* has seemed even more efficacious, and is much more pleasant to the patient. In *purpura hæmorrhagica* turpentine has been highly praised.

CHIAN TURPENTINE, the product of the Pistacia terebintha, has been very highly commended by Mr. John Clay as a remedy in internal cancer. I have known of its use in one case of uterine cancer, in which most astonishing results have followed its employment, and believe it should have a thorough trial. It is essential that the remedy be genuine; six grains of it may be administered three times a day continuously for many months.

DIGITALIS. U.S.

The leaves of the Digitalis purpurea, or fox-glove, of the second year's growth. These are large leaves, of a dull pale green, with whitish down underneath, and have a bitter nauseous taste and a faint narcotic odor. Digitalis yields both to water and to alcohol. M. Homolle discovered in it a peculiar bitter principle, which has been abundantly proven to contain the medical virtues of the crude drug, and, under the name *Digitalin* (DIGITALINUM), is now officinal in the U. S. Pharmacopœia. As prepared according to the directions of the latter, it is a whitish or yellowish powder, odorless, but of a very bitter taste, nearly insoluble in ether and in water, readily soluble in alcohol and in acids. With muriatic acid it makes a yellow solution, which soon changes to green. The officinal preparation is made by a process copied after that of M. Henry and M. Homolle. It crystallizes with great difficulty, and imperfectly. Nativelle, in 1871, announced (*Bulletin de l'Acad. Roy. de Médecine*, 1871, vol. xxxvi.) to the Academy of France that he had discovered a process by which crystallized digitalin could be prepared, and received the grand prize of Orfila.

Crystallizable digitalin (*Journal de Chimie Médicale*, 1873) occurs "in short and delicate needle-shaped crystals, and possesses an intense and persistent bitter taste. It is but slightly soluble in water, soluble in twelve parts of cold and six of boiling alcohol of 90°, less soluble in absolute alcohol, and nearly insoluble in ether; very soluble in chloroform. It is rapidly dissolved by a solution of chloral hydrate, the solution becoming greenish blue in color. The concentrated mineral acids dissolve it, hydrochloric acid producing an emerald-green color, sulphuric acid a green which if subjected to the action of bromine fumes changes to a dark red, nitric acid a yellow, nitro-muriatic acid a yellow changing to an obscure green, and a mixture of equal parts of sulphuric and nitric acids a rose color changing to a deep violet. When heated on platinum, it melts, swells up, becomes brown, and disappears without leaving any traces. It contains no nitrogen, but is composed of 51.33 per cent. of carbon, 6.85 per cent. of hydrogen, and 41.82 per cent. of oxygen."

According to Ch. Blaquart (*L' Union Pharmaceutique*, Nov. 1872), ten per cent. of crystallizable digitalin can be extracted from the crude drug, which probably contains twelve per cent. of it. The question whether this substance is the pure active principle of digitalis is of course an important one. The French commission reported as the result of physiological experiments that it produces in man and animals effects similar to those of the amorphous digitalin, but that it is much stronger than the latter. This conclusion has, however, met with some opposition. M. Gubler (*Bulletin de l'Acad. Roy. de Médecine*, vol. xxxvii. p. 404) denies that this crystallized digitalin is stronger than the amorphous preparation, and M. Vulpian in the subsequent discussion asserted that in experimenting he had found them of equal strength, and Ch. Blaquart (*loc. cit.*) in his experiments arrived at a similar result; yet one-ninth of a grain of it is said to have been given to an adult without causing a toxic effect.[*] Mégerand and Daremberg (*London Medical Record*, 1873, p. 278) have found the crystalline variety the stronger. Dr. Roucher affirms (*Gazette Médicale*, 1874) that the crystallized digitalin is readily convertible into the amorphous or granular variety; but he also asserts (*Les Mondes*, July, 1872) that it is a complex body.[†] This assertion is confirmed by several chemists, especially by O. Schmiedeberg (*Archiv für Experiment. Pathologie und Pharmakol.*, Bd. iii. p. 19), who affirms that there are in digitalin four active principles: *Digitoxin*, the most active of all, which constitutes the greater bulk of Nativelle's crystallized digitalin: *Digitalein*; *Digitalin*; and *Digitonin*.[‡] For a particular account of these substances the reader is referred to the paper of Schmiedeberg.[§] The only practical conclusion at present possible is, that it is best to use only officinal preparations, such as the tincture, which represent the crude drug.*

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[*] For the process of manufacture, see *Boston Medical and Surgical Journal*, p. 35, 1873.

[†] G. Bouchardat (*Bull. Thérap.*, xc. p. 81) calls attention to the fact that crystallized digitaline does not, and amorphous digitalin does, polarize light.

[‡] *Digitaliresin* and *toxiresin* are derivatives respectively from digitalin and digitoxin of Schmiedeberg. A study of their physiological action may be found in *Arch. Exper. Pathol. et Pharm.*, Bd. iv. p. 191.

[§] Consult also *Schmidt's Jahrbücher*, Bd. clviii. p. 234, for abstract of thesis by Nicolai Görz, of Dorpat.

PHYSIOLOGICAL ACTION.—To the therapeutist the interest in the physiological action of digitalis centres chiefly upon the circulation. The drug does, however, exert a direct influence upon the apparatus of voluntary motion which is worthy of notice. In toxic doses it lowers reflex activity, and induces lassitude, prostration, muscular tremblings, and sometimes convulsions. That the muscles themselves are affected has been proven by the researches of Vulpian, of Dybkowsky and Pelikan, and of Gourvat, all of whom have found that the muscles of frogs poisoned with digitalis respond more feebly than is normal to galvanic currents. The nervous tissue has, however, been found by Gourvat to be more susceptible than the muscular, the nerves losing their functional power sooner and more completely than the muscles.

As the result of an elaborate experimental study (*Reichert's Archiv für Anatomie*, 1871, p. 252), Dr. A. Weil concludes that digitalis first lessens reflex activity by directly—*i.e.*, independently of its action on the circulation —exciting the inhibitory reflex centres of Setschenow, and after a time by directly paralyzing the spinal cord. The experiments upon which this conclusion was based are divided into two series, in the first of which it was found that after small toxic doses of the poison great diminution in the reflex activity of the frog was apparent in from ten to twenty minutes, and continued until the death of the batrachian; but that this diminution for from twenty-five minutes to an hour was immediately suspended by section of the cord high up, the reflex activity returning at once to its normal state; that after large doses the reflex movements were almost abolished in five minutes, and continued until death, but at any time during the first ten or twenty minutes could at once be restored by section of the upper cord; that, both after large and small toxic doses, a time finally came when division of the cord had no power to restore the lost reflex functions. These experiments have been confirmed by Dr. Meihuizen (*Arch. für Physiolog.*, vii., 1873). The second of Dr. Weil's series of experiments were directed to discovering whether the action upon the inhibitory reflex centres and the cord was a direct one, or was simply the result of the altered circulation. In this part of the investigation, the hearts of frogs were cut out, or their motion arrested by the local application of a concentrated solution of the nitrate of potassium, or rendered slower by a dilute solution of the same salt, and the effects of these various procedures upon the reflex activity were studied. It was found that slowing of the heart's action did excite the Setschenow's centre, but not to nearly so great an extent as did digitalis, and that minute doses of digitalis sometimes stimulated the Setschenow's ganglion and lowered reflex activity before the heart was sensibly affected. In regard to the spinal cord it was proven that when the heart was killed by the local action of potash the reflex functions of the spinal ganglia remained intact for a much longer period than when digitalis was administered.

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* Digitonin is asserted to form the bulk of the soluble digitalin of commerce, and to be the same as *saponin*, the active principle of soap-bark. As saponin has been apparently demonstrated to be the physiological antagonist of digitalis, it is evident that the whole matter is exceedingly confused; and that the conclusion in the text is the only one that can at present be reached.

Circulation.—The action of digitalis upon the heart of the frog was, I believe, first investigated by M. Vulpian (*Comptes-Rendus de la Soc. de Biol.*, 1855, p. 70), who has been followed by numerous observers, among whom may be mentioned W. Dybkowsky and E. Pelikan (*Zeitschrift für Wissenschaft. Zoologie*, Bd. xi., 1862), A. B. Meyer (*Arbeiten aus dem Physiologischen Institut zu Zürich*, quoted by Boehm), Legros and Legroux (quoted by Gourvat), Claude Bernard (quoted by Gourvat), Rudolf Boehm (*Pflüger's Archiv für Physiologie*, Bd. v., 1872), Homolle (*Archives Générales de Médecine*, July, 1861), Gourvat (*Gazette Médicale de Paris*, 1871), Fothergill *Digitalis*, London, 1871), Fagge and Stevenson (*Tr. Royal Soc.*, London, vol. xiv.), J. F. Williams (*Arch. Exper. Pathol. und Pharm.*, xiii. 1), H. F. Gaskell (*Journ. of Physiolog.*, iii. 48).

The statements of these investigators agree in all essential points. One or two of them have occasionally noted a primary brief acceleration of the heart's action; but the rarity of its occurrence shows that it has been probably produced by some extraneous unnoted influence.

The first distinctive action of the drug is a marked lessening of the number of cardiac beats per minute, due to a prolongation of the diastole, which may be complete, but is more generally divided by an abortive attempt at ventricular contraction. The systole is abnormally energetic, so that the ventricles become white as the last drop of blood is squeezed out of them. As the action of the drug becomes more intense, the rhythm of the heart is very much affected, the ventricle and auricle no longer beating in accord. At the same time the diastole generally becomes imperfect, one portion of the ventricle maintaining its systolic spasm, while the rest dilates. Thus, the extreme apex may remain hard and white during the diastole, and even hernial protrusions of the ventricle may occur. Finally, the heart is arrested in systole; and as the muscle so hardens, of course all its power of responding to electrical or other excitants is lost.

In some rare instances, instead of the above series of phenomena, the diastolic periods throughout are prolonged and quiet, and after several periods of relaxation, lasting for ten or twenty seconds, final diastolic arrest may occur.

As both Boehm (*op. cit.*, p. 163) and Dybkowsky and Pelikan (*loc. cit.*) have found that the slowing of the heart's beat, the increased energy of contraction, the irregularity and final systolic arrest, are produced by digitalis after division of the vagi and destruction of the spinal cord, and as both Ackermann (quoted by Boehm, *op. cit.*, p. 158) and Boehm have found that the paralyzing of the peripheral ends of the vagi by atropia does not prevent the phenomena just alluded to, it is evident that the drug acts directly upon the heart-muscle itself, a conclusion which is confirmed by Eulenburg and Ehrenhaus (quoted by Dr. T. Lauder Brunton, *On Digitalis*, London, 1868, p. 51), who found that digitalis, when locally applied, acts at once upon the heart. On the other hand, the inhibitory activity of the peripheral ends of the pneumogastrics is without doubt increased by the drug. There is no stage in which stimulation of the vagi does not cause diastolic arrest. Indeed, Dybkowsky and Pelikan have seen galvanization of the nerves produce such relaxation in the auricles after the ventricles had already become permanently contracted. Further, Boehm has found that a stimulation of the pneumogastrics which is insufficient to make itself felt before poisoning will, after the exhibition of digitalis, cause diastolic arrest lasting for many minutes.

It appears, therefore, that the peripheral cardiac inhibitory apparatus shares in the stimulant action of digitalis; and as Boehm has found that diastolic arrest never takes place in frogs poisoned with the drug, after section of the vagi, it is probable that this rare mode of death is really due to super-excitation of the inhibitory cardiac nerves.

Rudolf Boehm (*op. cit.*, p. 170) has investigated the influence of digitalis upon the working power of the heart when freed from all connection with the central nervous system. By using the method of Ludwig and Coats, he obtained as a constant result that the amount of work done was increased by small doses of digitalis; that after large doses a similar increase was followed in a short time by very great diminution in the expenditure of power by the heart, a diminution apparently due to imperfect diastole and consequent non-admission of serum into the viscus. By direct experiment with an artificial circulation Dr. Williams has proven that the cut-out frog's heart actually puts out much more force than normal under the influence of digitalis. Dr. Williams believes that the increased work of the heart is largely dependent upon an altered tone of the muscle, producing a more complete diastolic enlargement of the ventricles. That the systolic arrest of the heart by digitalis is not of the nature of a paralysis but of a spasm is indicated by the fact that there are various paralyzing drugs which, applied to the contracted heart, will cause it to recommence its beat (Schmiedeberg, (*Beitr. z. Anat. u. Physiol.*, Festgabe, A. Ludwig). The experiments of François Frank upon the isolated apex of the heart appear to show that it is upon the muscle rather than upon the intra-cardiac ganglia that digitalis acts (*Journ. de Méd. de Bordeaux*, xi. 67).*

The elaborate experiments of L. Traube (*Gesammelte Beiträge zur Pathologie und Physiologie*, Bd. i., Berlin, 1871) upon warm-blooded animals showed that in dogs moderate doses of digitalis produce increased ar pressure, with lowering of the rate of the cardiac pulsation. When doses were used, these phenomena were followed by increase of the p frequency and fall of the arterial pressure, which, however, did not mence at the same time, since the maximum pressure was not reached the pulse had risen above the original, normal point.

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* In apparent opposition to all this older evidence are the researches of Messrs. Donaldson and Stevens (*Journ. of Physiology*, iv.). For an elaborate discussion of this paper and for the reasons why I do not think it should change our views, see editorial in *Therap. Gazette*, February, 1884.

The experiments of Boehm, Brunton (*loc. cit.*), Gourvat (*loc. cit.*) of Kaufmann on soluble digitalin (*Rev. de Méd.*, iv.), are in accord those of Traube; so that it may be considered proven that in man moderate doses of digitalis produce rise of arterial pressure with dimin pulse-rate.

Prof. L. Traube has found that, after section of the vagi, digitalis warm-blooded animals, with rare exceptions, incapable of reducing the p rate, and, contrariwise, that when the pulse-frequency has been reduce the drug, section of the nerves causes an immediate and very marked ri the rate of pulsation. I believe Boehm* has experimentally confirmed as have also Kaufmann and Gourvat.

It has been suggested that the slowing of the pulse is due simply t increased arterial pressure, but Kaufmann (*loc. cit.*, p. 389) has notice slowing of the pulse without rise of the arterial pressure, and it ap to me demonstrated that digitalis stimulates the cardiac inhibitory ne apparatus. The experiments of Kaufmann seem to show that in the mals there is not at any time under the influence of digitalis an incr susceptibility of the peripheral vagi; and it is probable that it is the i cardiac inhibitory centres rather than the fibres of the vagi which are upon. The occasional reduction of the heart-beat in warm-blooded anima digitalis after section of the vagi (Traube, Kaufmann) shows, however, e that the inhibitory nerves in some animals find another path than the p mogastrics, or else that there is an additional—sometimes inoperative, s times efficient—cause of the reduction of the pulse-rate. As it has shown that digitalis is capable of slowing the beat of the isolated hea the frog, it probably exerts a similar influence at times, in mammals, the cardiac muscle or its inhibitory ganglia.

Although digitalis does increase the muscular energy of the heart, it s scarcely possible that the enormous rise of pressure produced by it ca owing to this alone. This *a priori* reasoning has received experim confirmation from Malan,† Fothergill (*loc. cit.*), Gourvat (*loc. cit.*), A mann (*Ueber die Wirkungen der Digitalis*, in *Volkmann's Sammlung l scher Vorträge*, No. 48, Leipsic, 1872), and Boldt (*Inaugural Disserta Schmidt's Jahrbücher*, March, 1872). The first three of these investig have found that the arterioles of the frog's web as seen under the m scope undergo very decided contraction after the systemic use of digitalis; and Ackermann states that if the abdomen of a rabbit be opened so as to expose the arteries of the mesentery, a very marked contraction, even to the partial obliteration of the lumen of the vessels, can be readily seen to follow the exhibition of digitalis.

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* His language is such as to leave the point somewhat doubtful. *Op. cit.*, pp. 18

† Quoted by Fothergill (*op. cit.*).

Boldt experimented upon curarized frogs after the manner of Cohnheim, and found that the first effect of the digitalis was marked contraction of the arterioles.

It is stated by Kaufmann that in the latter stages of digitalis-poisoning the peripheral vagi are paralyzed so that galvanic stimulation of their trunks is powerless to affect the heart. This appears to be in opposition to all previous observations, and therefore must be confirmed before acceptance.

According to Boehm, Traube found that, if the spine be divided, digitalis is powerless to increase the arterial pressure, although lessening, as usual, the pulse-rate. The same authority also states that Bezold has seen an excessive fall of the arterial pressure ensue immediately upon the division of the spinal cord in an animal under the influence of digitalis. Further, in his own experiments Boehm has attained similar results, or, in other words, has found that after separation of the small vessels from the vaso-motor nerve-centre, digitalis does not increase arterial pressure.

These experiments would seem to prove that digitalis acts upon the vessels by stimulating the vaso-motor centres in the base of the brain; but they have been contradicted by Ackermann (*op. cit.*, p. 397), who states that he has many times cut the spinal cord and without exception found a very marked rise of arterial pressure follow the injection of digitalis. Unfortunately, none of these experiments have, that I am aware of, been published in detail, and it is therefore impossible to analyze or to reconcile them; but Görz (*Schmidt's Jahrbücher*, Bd. clviii.) expresses the opinion that Ackermann did not fully divide the cord in his experiments. Görz himself found that a rise is produced by digitalin after division of the cord, but of so small an amount as to be readily accounted for by the increased power of the heart.* Dr. J. F. Williams (*Arch. Exper. Pathol. u. Pharm.*, xiii. 1) has also found, after reduction of blood-pressure to zero by chloral, that digitalis will cause rise of pressure. This does not, however, throw much light upon the vaso-motor action of the drug, because by enormous doses of chloral the heart is almost as much affected as is the vaso-motor system. Drs. Brunton and Meyer (*Journal of Anatomy*, p. 138) injected digitalin into the ear of a rabbit whose cervical sympathetic and pneumogastrics had been destroyed, but were unable to obtain any satisfactory result; there was certainly no constant perceptible contraction, although sometimes the vessels were seen to empty themselves more rapidly than before the injection. By consentaneous, independent researches, Dr. Ringer and Sainsbury (*Medico-Chir. Trans.*, lxvii.), and Messrs. Donaldson and Stevens (*Journ. Physiol.*, iv.), using the method of Gaskell more or less modified, have apparently proven that digitalis acts upon the walls of the arterioles. They destroyed the nerve-centres of a terrapin; excised the heart and connected bottles in such a way with the blood-vessels that liquids would run through the arteries and come out through the veins. Under such circumstances they noted a marked reduction of the rate of flow when soluble digitalin was placed in the artificial serum. The wisest conclusion which can be drawn from our present evidence is that the drug probably acts *both upon the vaso-motor centre* in the medulla and *upon the walls of the arterioles.*

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* A similar rise has been observed by Kaufmann, who does not, however, give the extent of it (*loc. cit.*, p. 406).

It has been shown that the dichrotism in the frog's pulse is due to an attempted diastole before the systolic impulse has yielded; and Kaufmann has determined that in the mammal a similar partial relaxation, arrested by a renewed very brief systole, occurs and gives origin to a double pulse. Kaufmann has also noticed that a tendency to cardiac tetanus is manifested in the horse, as in the frog, under the influence of digitalis; but that in the former animal a permanent, complete cardiac spasm never occurs. He has further experimentally determined that the diastolic, as well as the systolic intra-ventricular pressure, is increased; but that the diastolic intra-auricular pressure is slightly diminished. If it should be hereafter proven that these are constant phenomena, it would appear that the drug acts upon the ventricles rather than upon the auricles.

The following proposition expresses our present knowledge, and probably is very close to the truth:

Digitalis in moderate doses stimulates the muscular-motor portion of the heart (probably its contained ganglia), *increases the activity of the inhibitory apparatus*, and *causes contraction of the arterioles*, probably by an action on the vaso-motor centres in the cord, and also upon the walls of the arterioles. As a consequence of the first action, the cardiac beats become much stronger; as the result of the last, there is narrowing of the blood-paths, and to the passage of the vital fluid an increased resistance, which, acting on the already excited inhibitory system, aids in the slowing of the pulse.

According to my own experience, decided therapeutic doses of digitalis, in man as in other mammals, produce great reduction and sometimes dicrotism of the pulse, and increase the size and force of the wave; at the same time the arterial tension is augmented. Poisonous doses induce, after a time, increase of the pulse-rate, with smallness and weakness of the wave and lowered arterial pressure.

Sphygmographic studies of the effect of digitalis upon persons suffering from various acute and chronic diseases have been made by M. Legroux, M. Bordier (*Bulletin Thérapeutique*, 1868, p. 110), Constantine Paul (*Bulletin Thérapeutique*, 1868, p. 193), and Paul Lorrain (*Journal de l'Anatomie et de la Physiologie*, 1870). The problems offered by these gentlemen are so complex as to render a detailed study almost impossible; but, as a whole, their tracings seem to confirm my personal experience. Paul Lorrain calls attention to the fact that when the drug has reduced the pulse-rate very greatly a second abortive systole can, on auscultation, sometimes be heard occurring during the long diastole, and some of his sphygmographic tracings are markedly dicrotic. It is evident that in man the second systolic movement occurs precisely as in animals; and it seems very certain that the proposition framed for the lower mammals applies also to man.

When the pulse has been reduced by digitalis to forty or fifty a minute the change from the recumbent to the erect position will not infrequently suffice to alter at once its character, so that it will become feeble, small, and one hundred and fifty per minute. The explanation of this seems to be that the heart of such a patient is just in the position in which the diastolic impulse is being overcome by the excessive systolic stimulation of the drug. Whilst the patient is recumbent, the line is not passed over, but the additional stimulation of the erect position carries the heart beyond the limit of regular diastole, and the over-effects of the drug are at once manifested.

The influence of digitalis upon the urinary secretion in health has been studied by numerous observers, with such diverse results as to prove that the action of the drug on the kidneys is so inconsistent and varying as to render it probable that it is in great measure indirect rather than direct. Thus, Jörg, Hammond (*Proc. Biol. Dept. Acad. Nat. Sciences*, Phila., Dec. 1858), and Brunton (*loc. cit.*) have found the secretion more or less decidedly increased, and Homolle (*Archives Générales*, July, 1861), Winogradoff (*Virchow's Archiv für Anatomie*, Bd. xxii., 1861), Stadion, and, according to Brunton, also Krahmer, Kluyskens, Vassal, and Shohl, have found it either uninfluenced or diminished. Kaufmann has found it uniformly diminished in the dog (*loc. cit.*, p. 411).

The urea in the apparently very careful experiments of Winogradoff (*loc. cit.*), of Stadion (*Prager Vierteljahrschrift für die Praktische Heilkunde*, 1862, Bd. lxxii.), and of Hammond (*loc. cit.*), was diminished, while in the almost equally elaborate experiments of Brunton (*loc. cit.*) it was increased. All four observers noted lessening of the chlorides. Mégerand, using the crystallized digitalin of Nativelle, found his urine increased twenty-five per cent. but his urea diminished twenty per cent. Auguste Meusnier has sought without success for sugar in the urine both of patients taking large doses of digitalis and of rabbits poisoned with the drug (*L'Action de la Digitale sur la Fonction glycogénique*, Paris Thesis, 1868). M. Kaufmann (*loc. cit.*, p. 413) states that digitalis leaves, or preparations which produce local irritation, cause in the dog an increase in the elimination of urea; but when digitalin is given in solution, so as to avoid all local irritation, the excretion of urea is diminished.

It is very certain that *toxic* doses of digitalis lower the temperature a number of degrees in healthy men and animals. It would seem, however, that the fall of temperature is generally, if not always, preceded by a rise, as has been noted by Bouley and Reynal, by Duméril, Demarquay, and Lecointe (quoted by Brunton), by Hirtz, by Legros (*Thèse*, 1867, quoted by Gourvat), and by Gourvat (*Gazette Médicale de Paris*, 1871, p. 572). Kaufmann believes that such rise is due to the local irritation produced by the drug, and asserts that if no irritation be produced there is always in the animal a fall of rectal temperature (0.4–0.5° C.) after even a feeble dose of digitalin.

The effect of *therapeutic* doses in the normal condition has not been closely studied, that I am aware of. But in a number of cases, chiefly of pneumonia, Z. E. Coblentz (*La Digitale comme Agent antipyrétique*, Strasbourg Thesis, 1862) found that about twelve hours after the fall of the pulse there was also a fall of temperature. The tendency of our present knowledge is to connect the changes in temperature induced by digitalis with the changes of the circulation; and it seems very possible that therapeutic doses in health will be found to increase bodily heat, although in fever they may diminish it.

THERAPEUTICS.—The chief clinical use of digitalis is in diseases of the heart; and from what has been said in regard to its physiological action it logically follows that it should be useful in loss of cardiac power.

When the muscle of the heart is for any reason unequal to the task set it, the systoles become rapid and imperfect, and by this irregular action the ventricles, neither completely filling nor emptying themselves, increase the embarrassment. Under these circumstances, digitalis, by lengthening the diastolic pauses and increasing the force of the systolic contractions, causes the ventricles to fill themselves in the one and to empty themselves completely in the other act. By subduing irregular action through the inhibitory nerves, by energizing the muscular power of the heart-walls, the remedy is of incalculable service, and, increasing arterial tension all over the body, causes the disappearance or lessening of symptoms due to low pressure in the arteries.

It is a logical necessity, if our reasoning as to the physiological action of digitalis has led to a correct result, that the drug should be of the greatest service when the lesion is simply loss of cardiac power; and clinical experience tallies with this *a priori* argument. In *simple dilatation*, or in *simple failure of the cardiac muscle* without valvular lesion, the results of the use of digitalis are most favorable.

On the other hand, in *simple hypertrophy* digitalis does harm, and should never be used. It must be borne in mind that although this agrees with what the experimentalist has proven to be the action of digitalis, yet it was discovered independently as a clinical fact by practitioners. Thus, Niemeyer, who ridiculed experimental therapeutics because he would not take the trouble to study them deeply and practically and was therefore incapable of understanding them,—Niemeyer says, "Digitalis in pure uncomplicated hypertrophy is unsuitable."

Valvular lesion of the heart, as is well known, gives rise under unfavorable circumstances to dilatation, but in favorable cases to hypertrophy, or rather in the great majority of cases to hypertrophy with dilatation. Following out the principles already inculcated, it might seem at first that the use of digitalis in hypertrophied hearts with valvular lesion ought to be reprobated. But it is known clinically that digitalis often does good in valvular lesion with enlargement of the heart. The results of logical deductions from our physiological conclusions as premises are, however, not really at variance with this. It must be borne in mind that structural and functional hypertrophy are different things: by this is meant that although a heart be enlarged and absolutely stronger than normal, yet it may be, relatively to the work required of it, *weak*. Thus, if 1 represent the normal work of the heart and 1 its normal power, if the former be increased to 4 and the latter to 3 the heart is really in the position of a weak organ, although possessed of three times its original strength. Hence it is that digitalis is often useful in valvular disease with hypertrophy. In the vast majority of cases the heart with diseased valves is in the position just spoken of; but sometimes the work advances only to 2 and the strength to 3; then the hypertrophy becomes excessive, and digitalis will increase the difficulty. In almost all cases the increased power of hypertrophy, unless the muscle be degenerated, renders effectual smaller doses than can be used in dilatation, and also increases the danger of the over-action of large doses.

In *mitral insufficiency* and in *mitral stenosis* digitalis is often of great service. It is evident that in both instances the valvular lesion leads as its first result to pulmonic hyperæmia. How does the digitalis lessen this? In the case of *stenosis*, the diastole being lengthened by the remedy, the auricle is afforded more time to empty itself into the ventricle through the narrowed orifice, and at the same time is strengthened in its contracting power; evidently, then, the left ventricle when its systole occurs will have much more to contract on than before the digitalis was administered, and the amount of blood in the systemic circulation will be increased,—*i.e.*, the amount in the pulmonic circulation will be diminished; further, the right ventricle will have greater power afforded it to force the blood through the lungs,—*i.e.*, to resist the recoil from the left auricle to which the impeded valve gives origin.

In *mitral insufficiency* the mechanism is different, but the result is the same. The increased power of the systole will throw proportionately more blood through the aortic orifice than through the partially open valve. The opening at the insufficient mitral valve is much smaller and more obstructed than the aortic orifice. As the force or rapidity of the current increases under the action of digitalis, the friction becomes greater at both orifices, but the ratio of increase is evidently far higher in the small choked mitral leak than in the wide aortic opening. Hence the large orifice constantly gains upon the smaller as the cardiac force is increased, and, more blood passing into the systemic circulation, the pulmonic is relieved. Again, the right ventricle shares the stimulant action of the drug, and acts more strongly upon the pulmonic circulation, resisting the direct backward flow from the auricle. There are cases of mitral cardiac disease in which digitalis seems to be indicated, but when given acts unhappily. In some of these cases the augmented distress is probably caused by a strain upon the auricles. If the ventricle be already too strong for the auricle, and if by virtue of a very patulous mitral valve the backing of the blood upon the auricle is very easy, it is readily understood how increasing the power of the ventricle may augment the auricular strain. Especially is this consideration important in the light of Kaufmann's researches, which seem to show that the ventricle is more affected by digitalis than is the auricle.

In *aortic constriction* digitalis is useful when the heart-power begins to fail. In these cases compensatory hypertrophy, with slowness of action, is very apt to occur, or even to become excessive: much more frequently does this happen than in mitral disease. Again, in *aortic insufficiency* the prolonged diastole of digitalis action favors the return of blood to the heart, and is not advantageous. It is evident that digitalis is not so generally useful in aortic as in mitral disease, nevertheless when the heart-muscle fails, and the hypertrophy is not compensatory, the drug is useful in both aortic stenosis and insufficiency.*

From the considerations which have been brought forward, it is very evident that a knowledge of the relation of the heart-muscle to the work required of it in any individual case is much more necessary to the therapeutist than to know what valve is diseased.

In "*irritable heart*" of soldiers, a disease or condition of cardiac irritability evidently connected with muscular weakness, and very probably dependent upon exhaustion of the inhibitory nerves, Dr. Da Costa (*American Journal of the Medical Sciences*, Jan. 1871) found that in the early stages of the affection digitalis not only acted better than any other remedy, but even, when administered continuously for some time, often effected a permanent cure. When hypertrophy had taken place, the drug was of little use.

The relief afforded by digitalis in not too inveterate cardiac disease is often in a measure permanent, because the drug may aid very materially in the production of compensatory hypertrophy. Dilatation is certainly more apt to occur when the muscular fibre is lax and acting feebly than when it is toned up and in vigorous play; secondly, the stimulus to action in a muscle is almost of necessity directly or indirectly a stimulus to its nutrition; lastly, and most important, improved systemic circulation means in a far more intense degree improved blood-supply to the cardiac muscle, as is shown by the following considerations.

During systole the cardiac muscle contracts so as to squeeze out completely all the venous blood from the heart-walls. The arterial blood enters during diastole, and the force which drives it into the relaxed walls is derived from the arterial system. The coronary arteries arise nearly at a right angle to the aorta: the blood squirts into the latter during systole in an unbroken stream, and of course does not enter the coronary artery. But when the reflux wave comes, the aortic valve flaps to, and the whole pressure of the blood-column forces the liquid into the open cardiac arteries. If the arterial system be empty or nearly so, the arteries are not distended sufficiently to give origin to a powerful reflux wave, and but little blood enters the coronary artery, *i.e.*, the cardiac walls. The dilated feeble heart is unable during systole to free its walls thoroughly of venous blood, and during diastole the force is lacking for driving in the arterial blood. Digitalis enables the cardiac muscle to free itself thoroughly of venous blood, and at the same time, by restoring to a greater or less degree the normal balance of the circulation and removing the excess of blood from the general venous system, gives the aorta sufficient blood to provoke an active reflux.

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* Consult Fothergill, *Antagonisms of Medicines*, Philad., 1878, p. 85.

If in *aneurism*, or in general *capillary atheroma*, there be increased resistance to the circulation, and the heart have not sufficient power to meet this, digitalis may be useful, but must be employed with caution. It undoubtedly increases arterial pressure; and this increased pressure may prematurely rupture an atheromatous cerebral capillary or tear open the thinned wall of an aortic aneurism. The use of digitalis for the purpose of "quieting the circulation" in aneurism is of very doubtful expediency. I have seen immediately fatal hemorrhage produced thereby.

In *cardiac dropsy* digitalis is of service probably not only by regulating through the heart the circulation, and by evacuating the surplus fluid through the kidneys, but also by an action upon the vessels. Clinicians do not allow enough for the *rôle* of the vaso-motor nerves in dropsy. Without saying more as to the clinical side of this question, which I have discussed elsewhere (*American Journal of the Medical Sciences*, July, 1871), it may be allowable to allude to the experiments of Ranvier (*Comptes-Rendus*, 1869, p. 1327), who found that when the vena cava was tied in a dog, and the sciatic nerve of one side cut, œdema occurred only in the leg whose nerve was divided.

The use of digitalis in large doses as a cardiac stimulant in *syncope* or in *sudden collapse* from hemorrhage or other cause is in its infancy. One or two cases have been reported in which the happiest results have followed its exhibition (case, *Pacific Medical and Surgical Journal*, 1874, p. 273), and it has been given hypodermically with the most astonishing effects in a number of cases in my wards at the Philadelphia Hospital. From twenty to thirty minims of the tincture should be injected into the arm, and repeated in half an hour if absolutely necessary, or one-fiftieth of a grain of the digitalin may be substituted. In my experience* the digitalin has several times given rise to severe local irritation, the tincture never.

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* Local irritation, and even the production of abscesses, has also been noted by various observers besides myself. See Witkowski, *Deutsches Archiv Klin. Med.*, xviii. p. 142; also Pel, *Centralb. Med. Wiss.*, 1877, p. 169.

Closely allied to the last use of digitalis is its employment in *poisoning* by substances such as *muscaria*, *delphinia*, and *aconitia*, which arrest the heart in diastole. Boehm has shown (*Pflüger's Archiv*, Feb. 1872) that in digitalis-poisoning of the frog, even when systolic cardiac arrest has occurred, these substances will often restore the cardiac movements,—a proof that real antagonism exists in their action; and Dobie reports a case (*British Medical Journal*, Dec. 1872) of recovery after the ingestion of an ounce of Fleming's tincture of aconite, apparently due to the hypodermic injection of twenty minims of tincture of digitalis and the exhibition by the mouth of three doses in an hour of a mixture of tincture of digitalis (one drachm each dose), brandy, and ammonia.

Digitalis is often of great value in various acute diseases,* such as *adynamic pneumonia* and *adynamic fevers*, by maintaining the heart's action. It can have no effect upon the diseases themselves, but may help most opportunely to sustain the heart during a crisis or a period of strain upon it.

With the idea that digitalis is an active *antipyretic*, it has been prescribed in various acute diseases, sometimes with asserted good results. As already stated, toxic doses of digitalis at first elevate the temperature; and proof is wanting that in healthy men therapeutic doses have any decided influence in depressing the temperature. There is, therefore, no good physiological basis for the antipyretic use of digitalis; at the same time, it is very possible that it may directly or indirectly lower the temperature in disease. Clinical proof of this is, however, still wanting. The strongest evidence in favor of such action is furnished by the records of Prof. Wunderlich (*Manual of Medical Thermometry*, Sydenham Soc. Translation, p. 325), according to which from half a drachm to a drachm of digitalis, given in divided dose during three or four days in the second or third week of severe *typhoid fever*, immediately produces a slight fall of temperature in a large proportion of the cases, and sometimes a considerable fall. This fall is said not to last more than a day, when the temperature rises again, but in cases favorably affected does not regain the original height; the pulse is very much lowered in frequency, and remains about uniform for four days. It is evident that at least in some of these cases of Wunderlich's the drug was given about the time natural defervescence would be expected to occur, and that the slight reduction of temperature brought about at such time does not argue very strongly in favor of the proposition that digitalis is a powerful antipyretic in disease. Far more extensive and complete observations must be made upon a rising, not a falling, temperature, before any satisfactory conclusion can be reached. At present the antipyretic use of digitalis should be purely tentative. In *puerperal fever*, Winkel (*Philad. Med. Times*, 1874, iv.) believes digitalis does good by its action on the circulation, by contracting the arterioles of the uterus and by lowering temperature.

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* Consult Hankel, *British and Foreign Medico-Chirurgical Review*, xxxi. 513; Grimshaw, *Dublin Quarterly*, June, 1873; Anstie, *London Practitioner*, Sept. 1873.

The property of causing contraction of all unstriped muscular fibres has been attributed to digitalis, and whilst the probabilities are certainly such as to invite investigation, yet we have no definite knowledge upon the subject. Mr. Dickenson (*Med.-Chir. Trans.*, vol. xxix.) claims that it has a powerful action in causing the uterus to contract and to arrest hemorrhage,—a few minutes after an ounce and a half of the infusion is swallowed in menorrhagia, severe pains resembling those of the first stage of labor coming on, with a momentary profuse discharge of blood and clots, if there be any present, followed by arrest of the flow for hours. Stadion (*Sydenham Soc. Year-Book*, 1862, p. 451) claims that digitalis is capable of temporarily but completely annulling the activity of the sexual organs, and that it may be regarded as a true anaphrodisiac. M. Gaunot (*Philad. Med. Times*, iv. 30) makes the same assertion, and advises the use of the drug in spermatorrhœa.

The use of digitalis as a diuretic will be considered under that heading.

TOXICOLOGY.—In poisoning by digitalis, the first symptom of any severity is generally vomiting of mucus and bile, very violent and very often repeated. At the same time a feeling of heat of the head, disordered vision, and vertigo manifest themselves. The pulse at this time in the horizontal position may be full and strong and slow, but on the patient's rising becomes weak and rapid. The face is pale. The vomiting continuing, profound prostration comes on, the pulse becomes feeble, small, irregular, although the beat of the heart may be strong and hard. The eyes are very prominent, the pupils fixed and dilated: according to Tardieu, an almost diagnostic symptom is the blue color of the sclerotic. Abundant salivation sometimes occurs. Intense headache and pains in the back or limbs are often complained of. Diarrhœa is very generally present; the urine may be suppressed. The intelligence is often perfect in the midst of profound collapse, but delirium more or less violent finally comes on. Death, usually preceded by stupor or by convulsions, takes place most frequently in one or two days, but has occurred as late as the tenth day, and as early as three-quarters of an hour.*

In the majority of cases of digitalis-poisoning the patient recovers. When this happens, the symptoms gradually ameliorate. Cardiac weakness, and even a *bruit de souffle*, with more or less exophthalmos, is said to have persisted for weeks in some cases. In poisoning by digitalin the symptoms are those of rapid digitalis-poisoning,—violent vomiting, intense cephalalgia, and sometimes rachialgia, irregular, feeble, intermittent pulse, paroxysms of suffocation.

The minimum fatal dose of digitalis is not known. A large teaspoonful of the tincture is said to have caused alarming symptoms in a young puerperal woman (Tardieu, *Clinique*, p. 685, Obs. VIII., Paris, 1867); twenty grains of the extract proved fatal on the tenth day (*Ibid.*, Obs. VI.); and two and a half grammes of the leaves in infusion on the fifth day (*Ibid.*, Obs. X.); fifty granules (gr. one-fiftieth each?) of digitalin have been recovered from (*Ibid.*, Obs. XII., XIV.); about one-fourth of a grain of digitalin (*Gazette Hebdomadaire*, July, 1874) produced very violent but not lethal symptoms. In the only fatal case of digitalin-poisoning I know of (*Affaire Couty de la Pomerrais*), the amount ingested was unknown.

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* See case reported by M. Barth, quoted by Tardieu. In a case of poisoning by ten grammes of tincture of digitalis, said to contain twenty milligrammes of digitalin, the symptoms were vomiting, great pain in the head, prostration, a very small pulse,—forty per minute,—anuria, and a systolic bruit heard over the whole heart, having its maximum intensity at the base. Recovery occurred in two days (*Mém. Soc. de Méd. de Bordeaux*, 1884, 397).

The treatment, after the evacuation of the stomach and bowels, and the very free administration of tannic acid, as the best, although unreliable, chemical antidote, should consist in the exhibition of opium, of alcoholic stimulants, and rest in the horizontal position. I know of no recorded experiences with the antagonistic poisons to digitalis, such as aconite or muscarin. As it is possible that whilst so far as the heart is concerned they may be really antagonistic and yet may intensify the action of digitalis on the cord, their use requires caution.

Two cases, one ending fatally, of what may be considered *chronic digitalis poisoning*, have been reported by Dr. Köhnhorn (*Lancet*, 1876, i. p. 583). The symptoms were loss of appetite, tinnitus aurium, vertigo, lowering of the rate and force of the pulse, diarrhœa, weakness, general anæmia, and syncopal attacks. The only lesion found at the autopsy was congestion with ecchymosis of the gastro-intestinal mucous membrane.

ADMINISTRATION.—Digitalis may be given in substance in the form of pills; the dose being one grain three times a day, and increased until some effect is produced. The solid *extract* (*Extractum Digitalis*, U. S.) is less reliable than the leaves; its dose is one-fourth of a grain. When a rapid action is desired, one of the following officinal preparations, or the digitalin, should be used: *Infusum Digitalis* (1 to 66.6),—dose, one fluidrachm to half a fluidounce; *Tinctura Digitalis* (1 to 6.66),—dose, five to twenty drops; *Extractum Digitalis Fluidum*,—dose, one to two drops. *Abstractum Digitalis.* U. S.—*Abstract of digitalis* is a good preparation, twice as strong as digitalis itself, and to be given in half the dose.*

In emergencies where single large doses are administered they may be very much larger than those here given. Thus, of the tincture two fluidrachms or even half an ounce may be exhibited; of the infusion, a wineglassful.

When digitalis is administered persistently, its first evident influence may be suddenly developed after long delay (case, *Philad. Med. Times*, vol. ii. p. 24). It is said that sometimes the first marked symptom of this so-called cumulative action is severe syncope followed by paraplegia, vomiting, diarrhœa, delirium, general insensibility, and death. Such cases must be extremely rare; usually a sudden drop of the pulse is the most serious effect, provided that the *administration of the remedy be at once suspended.* It is a matter of much importance to determine when this cumulative action is to be expected. It is probably connected with slow absorption and elimination, and is much more prone to occur when there is no diuretic effect. It is also very apt to appear after tapping; the sudden removal of pressure from the vessels leads to the picking up from the tissues of serum,—saturated, it may be, with digitalis principles,—and also to the rapid absorption of any digitalis which may be in the alimentary canal. Dr. T. Lauder Brunton and J. Theodore Cash (*Lond. Practitioner*, xxxiii. 272) find that high temperature so weakens the cardiac inhibitory apparatus in the cat that it will not respond to digitalis, and believe that this direct action of the bodily heat is in many cases of fever the reason why digitalis will not act. They caution against its too bold use in diseases with a sudden defervescence, because when the temperature suddenly falls, inordinate digitalis effects may appear. It should be a general practice in the persistent administration of digitalis to occasionally interrupt its use so as to allow a clearance of the system.

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* According to Fraenkel's experiments the most certain preparation of digitalis is the vinegar, then comes the infusion, and finally the tincture (*Charité Annallen*, 1881, 225).

Digitalin of commerce is a complex body of various composition, power, and even properties. There are two distinct varieties of it, one soluble, the other insoluble, in water. Much of the digitalin sold is inert, and especially is this true of "digitalin granules." As the preparation is complex, variable, and expensive, it has been dropped from the United States Pharmacopœia, and ought not to be used, especially as it has no conceivable advantage over the stable preparations of the drug. Even for hypodermic use the tincture seems preferable, as the digitalin solution appears to undergo change in a few hours, and usually causes more irritation when injected than does the tincture. The dose of digitalin is one-fiftieth of a grain.

CONVALLARIA MAJALIS.—In 1859 G. F. Walz discovered in this plant two active substances, *convallarin* and *convallamarin*. Of these the first is crystalline, insoluble in water, and, according to the experiments of Dr. W. Marmé (*Schmidt's Jahrb.*, Bd. cxxxiv. 166), when taken in doses of three or four grains, acts as a simple purgative. The glucoside convallamarin is soluble in water, and is the principle to which the plant owes its action upon the circulation. Marmé found that it kills by a direct action upon the heart, and in moderate doses first slows and then quickens the pulse: previous division of the vagi did not interfere with the development of these phenomena. The chief studies upon the physiological and therapeutic action of the lily of the valley are those of Prof. Germain Sée (*Bull. de l'Acad. de Méd.*, No. 27, 1882, p. 767) and of S. Isaew (*Hoffmann und Schwalbe's Jahrb.*, 1883, 122, from the Russian). Prof. Sée finds that in the dog it first slows the action of the heart and increases the blood-pressure decidedly, the respirations at the same time becoming fuller and a little less frequent. If a toxic dose has been given, the heart's beats become very rapid and irregular, the arterial pressure still being much above normal; finally, the pressure begins to fall, the cardiac pulsations to grow more feeble, and death occurs through syncope. It is stated that the pneumogastric nerves are weakened, but never paralyzed, whilst the general nervous system is not affected. In man the action of the drug upon the circulation is as in the lower animals, and there is said to be usually produced profuse diuresis and sometimes purging. In Isaew's experiments upon frogs with convallamarin, the heart was arrested in ventricular systole by two milligrammes of the pure convallamarin, the frog continuing to live for a long time, the remedy seemingly having no effect upon its general nervous or muscular system: isolating the heart had no effect upon the action of the poison. In the dog the phenomena of convallamarin-poisoning were as described by Prof. Sée, it being further noted that the pneumogastrics were not affected, that the pulse was often dicrotic during the stage of rapid cardiac action, and that the final arrest was diastolic, the heart-muscle not being able to respond to the most powerful galvanic stimulation. Dr. I. Ott has found that the cardiac arrest in the dog is systolic (*Archives of Med.*, Feb. 1883). In Drs. Coze and Simon's experiments the frog's heart was rendered slow and extraordinarily full in its beat and finally arrested in systole (*Bull. Gén. Thérap.*, cv. 494). G. Leubuscher (*Zeitschr. f. Klin. Med.*, vii. 582) finds that convallamarin produces in the frog progressive palsy, with cramp-like tremblings and death from systolic cardiac arrest; in the mammals, violent convulsions and death from diastolic heart-arrest; that it slows the heart-beat in the mammal, and causes arythmical contractions, but in no dose elevates at any time the arterial pressure. The evidence seems to be so contradictory as to suggest that different observers have used different principles under the one name.

The lily of the valley is said to have been long used by the Russian peasantry for the relief of dropsy, and in 1880 Drs. Troitzky and Bojojawlewsky called attention to it as a valuable remedy in *cardiac valvular* disease, especially when associated with *dropsy* (*Wratsch.*, 1880, 47). Prof. Sée recommends it in palpitation of the heart, in cardiac dilatation, fatty degeneration, and other forms of cardiac weakness, also in valvular lesions with failing heart-power; in a word, in the class of cases in which digitalis is now used. When there is dropsy, its very positive diuretic action renders it especially valuable, and in some cases it purges freely, probably through the convallarin. The value of the remedy has been confirmed by Prof. H. Desplats (*Journ. des Sciences Méd. de Lille*, Oct. 1882), and by several other practitioners. Although condemned after trial by Dr. B. Stiller (*Wien. Med. Wochenschrift*, Nov. 1882), by Pel (*Centralb. f. Therapie*, 1883), by Leyden (*Deutsch. Med. Wochensch.*, Feb. 1883), by Stiller, by Jacobi and Lubilinski (*Sitzungsb. der Vereins für inner. Med.*, 1883), by G. Leubuscher; it has been highly praised by Prof. Silvestrini (*La France Méd.*, October, 1883), and by E. Maragliana (*Centralb. f. Med. Wissens.*, 1883, p. 43), it should be further studied both physiologically and clinically. In cases in which it has failed the preparation used may have been a bad one. Dr. Marmé found that the fatal dose of convallamarin was, for the dog, 0.015–0.03 grm.; for the cat, 0.005 grm.; for the rabbit, 0.006–0.008 grm. Prof. Sée gives, of an aqueous extract of the whole plant, from fifteen to twenty-three grains a day; Bojojawlewsky, each day an infusion representing from fifty to one hundred grains of the plant.

CLASS IV.—CARDIAC SEDATIVES.

THERE are certain drugs which are used by practitioners to decrease the activity of the circulation; and it is these which are here considered under the heading of *Cardiac Sedatives.* Many, in fact all of them, possess other powers besides those which cause them to be considered under this caption, and none of them are in very close accord in these qualities. There is, however, a *general* resemblance in the action of such as are derived from the vegetable kingdom, in that they are all sedatives to the motor-nervous system and yet all produce convulsions. I have made an especial experimental study of these convulsions (*Philadelphia Medical Times*, vol. iii.), and have found that they are cerebral and not spinal, because they do not occur in any part of the body separated by section of the cord from cerebral influence. Further, they are probably due to disturbance of the circulation at the base of the brain, for the following reasons, the truth of each of which has been experimentally determined: first, lessening of the circulation at the base of the brain will cause convulsions; secondly, the convulsions produced by the cardiac sedatives do not occur until the arterial pressure is reduced about one-half; thirdly, if the disturbance of the cerebral circulation be artificially increased by tying the carotids previous to poisoning, or in any other way, the convulsions come on sooner and are more violent; fourthly, in some animals the convulsions caused by arresting circulation at the base of the brain are feeble and ill defined, whilst in others they are violent, and I have found that in species of the first order cardiac sedatives produce but slight convulsions, whilst in species of the second order they cause violent convulsions.

The indications for the use of a cardiac sedative may be said to be increased arterial excitement, sthenic fevers, and severe local inflammations. In order that a rational selection of the various drugs may be made for any individual case, it is necessary to study how, in these various conditions, relief is afforded by an arterial sedative. When there is arterial excitement from irritation, or excitement of the heart, the mode of relief is too obvious to need discussion. It is plain that in such a case a drug should be selected which simply depresses the heart's action and does nothing more. In sthenic fever the case is different; here it is desirable to relax the peripheral vessels and to promote a flow of blood to them, whilst the rapidity and force of the circulation is diminished. A drug which depresses the action not only of the heart but also of the superficial vaso-motor nerves is here indicated, and if to these powers is added a special one of stimulating the perspiratory glands, the most perfect remedy is obtained. With inflammation the effect desired is a lessening of the flow of blood to the part. A simple cardiac sedative may do this, by lowering the force of the circulation, but a cardiac vaso-motor sedative is far more powerful. The blood-vessels of the inflamed part are already dilated, and consequently attract blood, as it were, to the part. If the remedy dilates all of the blood-vessels this local attraction ceases, and blood is diverted from the inflamed tissue. It would appear from the experiments of Ludwig, Schiff, and others (*La Nazione*, Aug. 1872), that the blood-vessels, after complete dilatation, are able to hold twice the normal amount of blood, and Golz, quoted by Fothergill (*British Med. Journ.*, 1873), found the intestinal vessels were able to contain all of the blood of the body. These facts show how by means of an arterial sedative, which paralyzes the vaso-motor centres, "we can bleed a man into his own blood-vessels," or, in other words, get much of the effect of a venesection by drawing blood from the diseased part.

ANTIMONY.

ANTIMONII OXIDUM. U.S.—OXIDE OF ANTIMONY.

A grayish-white powder, insoluble in water, wholly soluble in muriatic or tartaric acid. It is prepared by dissolving the sulphuret of antimony in muriatic acid, adding nitric acid, and precipitating with water of ammonia. Its solution in the stomach is dependent upon the acid there present, and consequently, being uncertain in its action, it should not be used internally —although it is capable of producing all the effects of tartar emetic, for the preparation of which it was introduced into the Pharmacopœia. *Antimonii Sulphidum*, U. S., *Antimonii Sulphidum Purificatum*, U. S., and *Antimonii Sulphuratum*, U. S., are still more uncertain preparations, whose therapeutic use ought not to be encouraged.

ANTIMONII ET POTASSII TARTRAS. U.S.—TARTRATE OF ANTIMONY AND POTASSIUM.

Tartar Emetic is prepared by boiling the oxide of antimony in a solution of bitartrate of potassium. It occurs in the form of a white powder, the result of the pulverization of transparent, colorless, slightly efflorescent crystals, which are most commonly rhombic octahedrons. Its taste is variously described: to me it is at first very slight, but after a time styptic and acrid. In some persons it blisters the tongue and lips after a few moments of contact. Tartar emetic is insoluble in absolute, but soluble in dilute alcohol, soluble in from two to three parts of boiling water, and in from twelve to fifteen parts of water at ordinary temperatures. It is incompatible with alkalies and with acids, including tannic acid and substances containing it.

Physiological Action.—Locally applied, tartar emetic is an irritant, acting upon some very delicate and susceptible skins in a very short time.

In most instances, however, its continuous application for several days is necessary to produce any effect. At first there is simply a redness, accompanied by some burning pain and the eruption of small papules, which shortly become converted into vesicles and then into pustules. These are irregular in shape and size, varying from one-eighth of an inch to an inch and a half in diameter, and are very painful. Sometimes these pustules give rise to small sloughs, but generally, if the application be withdrawn, they simply give origin to superficial ulcers, which readily heal.

The only symptoms which are induced by small therapeutic doses (one-twelfth of a grain) of tartar emetic when exhibited for a short time are a scarcely perceptible diminution of the force of the pulse and an increase of the perspiration.

By somewhat larger amounts of the drug, nausea is induced, and is accompanied in a more decided degree by the phenomena just mentioned. After large doses, prolonged nausea, violent vomiting and retching, with marked reduction of the force of the pulse, great muscular relaxation, and a feeling of faintness, occur. At the same time the saliva is generally increased in amount, and the skin is bedewed with sweat.

After poisonous doses all these symptoms are intensified. The vomiting is violent, repeated, continuously re-excited by the slightest provocation, and is accompanied by burning in the œsophagus and stomach and by colicky pains in the abdomen. The matters vomited are first mucus, then mucus and bile, and finally, in some cases, blood. With the gastric disturbance occurs violent and frequent serous purging, the discharges resembling those of cholera, but becoming in some cases towards the last bloody. Cramps may occur in the extremity, and, in conjunction with the serous purging, have caused the antimonial poisoning to be mistaken for cholera. The exhaustion is extreme, and finally ends in collapse, with thready or imperceptible pulse, pinched, livid countenance, suppressed voice, profuse cold sweats, lowered temperature, and at last death from asthenia, generally preceded by stupor or convulsions: indeed, Taylor reports cases in which wild delirium was present some hours before death. The urine* in mild cases is increased in quantity, as it is also in the beginning even in fatal cases, but in such towards the close it is generally scanty and bloody, and even suppressed. C. Güthgens found, in some incomplete experiments, an increase of the elimination of urea after repeated non-toxic doses of antimony (*Centralbl. Med. Wiss.*, 1870, 321).

It is evident that the symptoms just enumerated can be best studied in detail under several heads. Before entering upon this, however, it is well to premise that the experiments of Viborg (*Stillé's Therapeutics*, vol.

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* What is said in the text is, I think, correct; although authorities differ on this point. Trousseau (*Traité thérapeutique*, 4th ed., vol. i. p. 619) affirms that it is suppressed; Husemann, that it *never* is suppressed (*Toxicologie*, p. 854); Tardieu, that it is scanty. For a case in which *it was suppressed*, see Taylor's *Medical Jurisprudence*, London, 1873, p. 309.

ii.), Buchheim, Courten (*Ibid.*), Magendie (*Ibid.*), Ackermann (*Virchow's Archiv*, Bd. xxv. p. 531), Richardson (*London Lancet*, May, 1856), Nöbiling (*Schmidt's Jahrbücher*, Bd. cxl. p. 24), and Radziejewski (*Reichert's Archiv für Anatomie*, 1871), and of others, have demonstrated that tartar emetic acts upon the lower animals precisely as on man.

Circulation.—When a sufficient dose of tartar emetic is injected into the frog (Radziejewski, Ackermann, Nöbiling), the cardiac contractions in a very short time are lessened in frequency and force, and become irregular, the auricles pulsating more frequently than the ventricles, until finally arrest occurs in diastole. After death the irritability of the cardiac muscle to ordinary stimuli is almost, or more frequently entirely, destroyed; but in the recent experiments of I. Soloweitschyk (*Arch. Exper. Path. u. Pharm.*, xii. 440), digitalis placed upon the paralyzed heart caused it to recommence its action; evidence that it is rather the excito-motor ganglia than the muscle fibre which is affected by the antimony. Upon the heart of the mammal the drug acts as upon that of the frog. According to the researches of Ackermann and of Ernst Sentz (*Experimenta de Ratione Interpulsus, etc.*, Diss. Inaug., Dorp. Livon., 1853), the arterial pressure always falls steadily and to an extreme degree. The pulse sometimes seems accelerated at first, but in the great majority of cases is decreased very decidedly in its rate. During this period of slow pulse the diastolic pauses are extremely long, but the individual beat will influence the mercurial column of the cardiometer five times as much as normal. After a while the pulse suddenly becomes very rapid, the force of the heart-beat is almost completely lost, the arterial pressure falls to a minimum, and in a very few moments diastolic arrest occurs. It is evident that the action of antimony upon the heart is a direct one. The irritability of the muscle is lost, and Ackermann has found that the cut-out heart of the frog is affected by the solution of tartar emetic; further, the experiments of Radziejewski have proven that the peripheral ends of the vagi in antimonial poisoning are early more or less completely paralyzed, so that the diastolic arrest cannot be due to excitation of the inhibitory apparatus.* The depression of the heart-muscle power does not seem, however, to be the sole cause of the lowering of the blood-pressure, for Soloweitschyk has found that galvanization of the vaso-motor centre with a powerful current is powerless to produce any elevation of the arterial pressure at a time when the heart still responds to stimuli. The conclusion is reached that antimony *lowers arterial pressure by a direct action upon*

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* Perhaps the present is as fitting as any other position to notice the theory of Nöbiling, that the action of tartar emetic upon the heart is owing to the potash it contains. This theory in itself is so improbable that it would seem scarcely worthy of discussion, were it not for the fact that Nöbiling asserts that the tartrate of antimony and soda is not poisonous. Dr. Radziejewski (*loc. cit.*, 485) has repeated and extended the experiments of Nöbiling and completely disproved both the asserted fact and the theory based upon it, showing that the soda-salt is as poisonous as the potash-salt.

the heart and the vaso-motor system, and that it is probably the peripheral portions of the latter system which are affected.

Nervous System.—A prominent symptom in antimonial poisoning is paralysis, affecting to an extraordinary degree the sensory and to a less extent the motor system. In man the anæsthesia which occurs in animals has been overlooked, but in the advanced stages of poisoning it is no doubt present. Radziejewski and Soloweitschyk have found that the depression of reflex activity occurs after section of the cord, and is therefore not due to stimulation of the Setschenow inhibitory centre; that it is not prevented by tying an artery and cutting off access of the poison to the nerve, and is therefore not peripheral. It consequently must be spinal, and as both observers noted that in the frog and the rabbit voluntary movements persist after the total abolition of sensibility and of reflex activity, the conclusion is reached that antimony is a paralysant to the *receptive centres or sensory tract of the spinal cord.*

Radziejewski states that sensibility is first lost towards thermic and chemical irritants, and then towards tactile stimuli. The motor nerves and muscles are said to retain their functional power.

Temperature.—The influence of antimony upon the temperature appears not to be very marked when the drug is exhibited in ordinary therapeutic doses. Thus, Ackermann found that, after doses severe enough to induce violent vomiting, no alteration in the temperature could be discovered by the thermometer under the tongue. Owing no doubt to the disturbance of nervous and arterial action, there is in these cases, however, a very marked reduction of the temperature of the extremities. Thus, in the cases just alluded to (Ackermann) the heat of the hands was lowered from 0.2° C. to 3.5° C. in various persons. This decrease of the temperature is certainly in a measure due to increase of the heat evolution.

After poisonous doses of antimony the decrease of animal heat is very perceptible, provided the victim live sufficiently long. Thus, in Ackermann's experiments a fall of only 1.6° C. occurred in rabbits killed in the hour, but in those that lived five hours the depression amounted to 6.6° C.

Abdominal Organs.—It cannot be gainsaid that tartar emetic acts as an irritant upon the alimentary mucous membrane. Although cases (*Archives Générales*, Sept. 1865) have been reported in which no lesion has been found in the stomach or bowels after death from antimony, yet in the great majority of instances very decided indications of violent inflammation have been present.

Dr. Radziejewski, on the strength of this action, and of two experiments in which he found the greater portion of the ingested antimony in the vomit of the patient, has advanced the theory that the emesis is due to a local action of the drug. The persistent nausea, however, certainly indicates that the remedy does not act like the so-called mechanical emetics. Further, the vomiting induced in the experiment of Magendie, of replacing the stomach of an animal by a bladder and giving tartar emetic, would seem at first sight to settle the point completely. This experiment of Magendie has been confirmed by Brinton (*Cyclopædia of Anatomy*, Supplement, p. 319; *London Lancet*, 1853, vol. ii. p. 599), who further proved that when tartar emetic was injected into the vein of an animal it was very freely and rapidly eliminated by the stomach. Dr. B. W. Richardson (*London Lancet*, vol. i., 1856) has corroborated this, and has also found that a similar elimination follows the inhalation of antimonietted hydrogen. I think, therefore, it must be conceded—first, that the finding of even a large quantity of antimony in the vomit does not prove that its action on the stomach is chiefly a local one; secondly, that the emesis is certainly preceded by at least a partial absorption. This would seem to show that the emesis is purely centric. The experiments of Mooso (*Schmidt's Jahrbücher*, Bd. 169, p. 236), on the other hand, indicate that the local action of the drug is a powerful factor in the production of the vomiting. It was found that when tartar emetic was administered by the mouth vomiting was caused by smaller quantities and more promptly than when injected into the veins; also that, after section of the peripheral vagi in the abdomen, a reverse relation existed between the two methods of administration. If these experiments be, as they appear, correct, tartar emetic must cause vomiting partly by an action on the centres and partly by a local influence upon the stomach The purging induced by tartar emetic is seemingly an effort at elimination.

Respiratory Organs.—The respiration in poisoning by antimony is very irregular, with all sorts of variations in the rhythm of the act. In the advanced stages the pauses are often very long, and the inspiration and expiration so forced and prolonged that very generally, in animals at least, marginal emphysema and subpleural ecchymoses are found after death. The origin of the respiratory trouble is probably somewhat complex, the chief factor being the direct influence of the drug upon the respiratory nerve-centres, and minor causes the intense venous congestion due to the failure of the circulation, and the alteration of the blood itself. Upon the mucous membrane of the lungs antimony acts directly or indirectly, even in moderate doses, as is shown by clinical experience and by the experiments of Mayerhofer (*Nothnagel's Arzneimittellehre*, Berlin, 1870, p. 219).

THERAPEUTICS.—There are three indications to meet which tartar emetic is constantly employed. The first of these it fulfils by virtue of its powers as *an emetic.* The discussion of this may be found in the chapter upon Emetics.

The second purpose for which antimony is used is to *depress arterial excitement.* It is chiefly in *inflammation* that tartar emetic is used as an arterial sedative. In combination with more decided diaphoretics it is constantly employed by some surgeons in *fever after operations*, in *gonorrhœa*, and in various sthenic inflammatory affections. In *pneumonia* it has been very largely used, forming an essential portion of the older plan of treating that disease. According to the method of Rasori, four or five grains a day were at first given, but rapidly increased to twenty-four or even thirty grains daily. Although by the aid of opiates and careful dilution a species of tolerance was often obtained for these heroic doses, yet very properly the plan has been abandoned by modern therapeutists. As tartar emetic if administered in sufficient quantity to depress markedly the circulation causes generally intense nausea and often purging, I think it is inferior to aconite or veratrum viride when it is desired to depress the circulation very decidedly in pneumonia or any other disease.

Owing to its action upon the mucous membrane of the bronchial tubes, in the first stages of *bronchitis* tartar emetic is an invaluable remedy. After free secretion has been established, other expectorants are, I think, of more service. The value of antimony as a *diaphoretic* depends largely upon its action on the circulation. Minute doses of it are constantly employed to increase the efficiency of fever-mixtures. It must always be borne in mind that it is a powerful depressant, and is therefore to be employed only in sthenic cases.

As a *counter-irritant*, tartar emetic is used only when it is desired to produce a slow, persistent, and at the same time very decided impression. For further discussion of its application to disease, see chapter on Rubefacients.

TOXICOLOGY.—The general symptoms produced by poisonous doses of antimony have been sufficiently described. There is, however, according to authors, a form of antimonial poisoning in which neither vomiting nor purging* occurs, the symptoms being simply intense prostration, cold clammy sweat, a sense of oppression in the chest, with the respiration at first increased, then diminished in frequency and embarrassed; a rapid feeble pulse, after a time becoming slow, intermittent, and irregular; delirium, unconsciousness, tremblings, and clonic and tonic convulsions (Husemann, *Toxicologie*, p. 853).

Tardieu (*loc. cit.*, p. 608) states that in some cases of tartar emetic poisoning a rash exactly resembling that produced by the external application of the drug has appeared all over the body on the fourth or fifth day.

As already stated, in the vast majority of cases there are to be found, after death from antimonial poisoning, very decided traces of inflammation of the stomach and bowels; in some cases, however, these appear to be wanting. The venous system is generally very much engorged, and the viscera are intensely congested. Magendie asserted that in animals poisoned by tartar emetic the lungs are always full of portions apparently hepatized; but Ackermann (*loc. cit.*, p. 544), in twenty experiments, found only some marginal emphysema and subpleural ecchymoses, with, in one or two cases, spots of atelectasis in the lungs. The assertion of Magendie, therefore, is too sweeping; but it is true that, in a large proportion of fatal cases of antimonial poisoning, emphysema, pulmonary apoplexy, atelectasis, or other structural lesions of the lungs exist. The blood usually coagulates imperfectly.

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* Husemann states this. Although vomiting is absent in these cases, purging is generally present. I do not remember to have seen the report of a case in which it was absent.

Dr. Saikowsky (*Virchow's Archiv*, Bd. xxxiv. p. 78, 1865), of Moscow, has found that when animals are fed upon antimonic acid (one-half to one gramme daily) or other preparations of the metal for from fourteen to nineteen days, the liver, kidneys, and even the heart undergo a fatty degeneration; also that there is a lessening of the amount of glycogen in the liver, and in some cases even a total disappearance of it. This has been confirmed by Profs. Grohe and Mosler, who state that in the duchy of Brunswick the peasantry give to the geese, when producing the famous fatty livers, a certain quantity of the white oxide of antimony every day.

The minimum fatal dose of tartar emetic is not known. Three-quarters of a grain in a child, and two grains in an adult, have proved fatal; but in the latter case extrinsic circumstances favored the result (Taylor, *Guy's Hospital Reports*, Oct. 1857, an analysis of thirty-seven fatal cases); two hundred grains have been recovered from (case, *Taylor's Medical Jurisprudence*, 1873, p. 309); also one hundred and seventy grains (*N. Y. Med. Rec.*, xxiv. 401).

Chronic Poisoning.—According to Mayerhofer (*Heller's Archiv*, 1846, quoted by Taylor), the symptoms following the criminal administration of small doses of tartar emetic at intervals are nausea, mucous and bilious vomiting, watery purging, often followed by constipation, small frequent pulse, and asthenia, deepening into death from exhaustion.

The treatment of antimonial poisoning consists in washing out the alimentary canal with large draughts of *tannic acid*,—the best known antidote,—and in the use of opium and of internal and external stimulants.

ADMINISTRATION.—The sudorific dose of tartar emetic is one-twelfth of a grain, the emetic dose one-half to one grain, repeated every twenty minutes as necessary. The *Antimonial Wine* (*Vinum Antimonii*, U.S.) contains two grains of tartar emetic in the ounce. The emetic dose is half a fluidounce. The *Unguentum Antimonii* (tartar emetic, one part in five) is employed externally, as a counter-irritant. A small quantity is spread upon a linen rag and laid upon the skin, or a little of it may be well rubbed in twice a day. Whenever it is persistently used, there comes on, sooner or later, a peculiar burning or tingling pain, which is very shortly followed by pustulation. The effect of the drug is very persistent as well as severe, so that the remedy is applicable only to a few cases in which an action of the kind spoken of is required. Care must be exercised not to continue the application too long, lest severe and obstinate ulceration be produced.

VERATRUM VIRIDE. U.S.

The root-stock of Veratrum viride, a coarse perennial herbal plant, indigenous to the Northern United States. It is a large tapering rhizome, an inch or two in length, less than an inch in thickness at the base, and having a bitter acrid taste. It contains two alkaloids, *jervia* and *veratroidia*, which are so closely associated with the resin as to be separated from it with great difficulty. The nature of these alkaloids has been the subject of much discussion among chemists. Mr. Charles Bullock was, I believe, the first to separate them one from the other, and to prove the inertness of the resin. In accordance with the belief of Mr. Bullock that these alkaloids were distinct from all previously discovered, Dr. George B. Wood named them *viridia* and *veratroidia*. Dr. Peugnet subsequently showed that viridia was identical with jervia, previously described by Simon, from veratrum album. Mr. Mitchell (*Proc. Amer. Pharm. Assoc.*, 1874) confirmed this, and concluded, with Peugnet and Bullock, that veratroidia is distinct from veratria. Recently (*Amer. Journ. of Pharm.*, 1876, p. 1) Prof. Wormley has arrived at the conclusion that veratroidia is identical with veratria. Without intending to deny the conclusions of Prof. Wormley, I shall, in the present edition, allow the text of the old edition to stand, so far as concerns the names employed to represent the two alkaloids of veratrum viride. *Jervia* is so closely united with the inert resin that it is separated from it with great difficulty.

PHYSIOLOGICAL ACTION.—In treating of the physiological action of veratrum viride, I shall first speak of the effects of its alkaloids singly. When an animal is poisoned with *jervia*, the first symptom manifested is sluggishness, as shown by a disposition to be quiet, accompanied by distinct signs of muscular weakness. In a little while peculiar rapidly-repeated thrills run through the muscular system, so that the animal trembles violently. After a greater or less length of time the animal becomes unable to stand, from weakness, and at or before this period violent convulsions appear,—general clonic spasms without rigidity. The convulsions alternate with intervals of relaxation, and as the animal grows more profoundly prostrated are less severe, but they continue in most cases up to death. Even when they are most violent, force is evidently wanting. The animal is totally unable to raise himself from the ground; the pigeon drives himself forward upon his breast, the rabbit pushes himself along on his belly, or lies upon his side and kicks into the air. Sensation appears to be benumbed only very late in the poisoning, and consciousness is preserved almost to the last. The pupils are not affected. There is no purging or vomiting, but always profuse salivation. Respiration ceases before cardiac action, so that death probably takes place from asphyxia.

The circulation is profoundly affected. The pulse is generally, if not always, lessened in frequency, *provided the animal be quiet*. When there are convulsions, or even when the tremors are marked, it becomes very rapid. The arterial pressure is greatly lowered, falling progressively from the beginning to the end of the poisoning. The force of the individual beat appears not to be much altered at first.

In an elaborate series of experiments (*Philadelphia Medical Times*, vol. iv.) I found that jervia had little or no effect on the pneumogastric nerves, since it acts as usual after those nerves have been cut, and galvanization of the par vagum in animals profoundly affected by the poison produced the usual cardiac results. Further, when the cord was cut very high up, so as to paralyze the accelerators, jervia still lessened the pulse-rate. As it was also proven that the alkaloid lessens the arterial pressure after division of the cord, *i.e.*, after vaso-motor paralysis, and also that it paralyzes the heart of the frog or turtle when placed directly upon it, it follows that jervia lowers the force and frequency of the cardiac beats independently of its nerves, by a direct action on the cardiac muscle or its contained ganglia. When the nerve-trunks were galvanized in an animal poisoned with jervia, although the pain-cries showed that the afferent nerves were not paralyzed, little or no rise occurred in the arterial pressure. It seems, therefore, that the jervia acts not only on the heart, but is also a powerful depressant to the vaso-motor nerve-centres.

In frogs, as well as in the higher animals, poisoned with jervia, there is a very marked diminution and finally abolition of reflex activity; and, as the functions of neither peripheral nerves nor muscles are interfered with, it is evident that the alkaloid is an intensely powerful spinal depressant. The convulsions are cerebral in their origin, as they do not occur below the point of section when the spinal cord is divided.* Locally, jervia is very feebly if at all irritant.

The general symptoms induced by *veratroidia* resemble those caused by its congeneric alkaloid, but it is decidedly more irritating than the latter, and always induces vomiting, and occasionally purging. In poisoning by it there are in most cases some muscular twitchings, and finally marked convulsions, but neither of these are so severe and so repeated as in the case of viridia. Death takes place from asphyxia, due to paralysis of the respiratory muscles.

Upon the spinal cord, the peripheral nerves, and the muscles, veratroidia acts very much as does jervia, being a decided spinal depressant.

The action of veratroidia upon the circulation is a very curious one. After a hypodermic injection of the poison the rapidity of the pulse and the arterial pressure are at first decidedly lessened. After a time, the pulse still remaining very slow, the individual heart-beats become endowed with a force greatly beyond normal, and the arterial pressure becomes normal; then suddenly the pulse-rate becomes very rapid, the individual cardiac beats losing much of their extraordinary vigor, but the arterial pressure rising nearly fifty per cent. beyond its original position.

When the alkaloid is thrown directly into a vein, these phenomena are intensified and abbreviated. I have seen the arterial pressure fall to zero in thirty seconds, and in one and a quarter minutes rise to 165 (110 normal) centimetres. The rise is not due to a direct action of the drug, but to the sudden asphyxia which it induces, since it does not occur if free artificial respiration be maintained (*Philadelphia Medical Times*, vol. iv.).

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* Some of the conclusions of my first investigation (*American Journal of the Medical Sciences*, 1870) of this drug were called in question, but I have in my last paper gone over the whole ground afresh. The earlier discussion may be found in the *Philadelphia Medical Times*, vols. ii. and iii.

When artificial respiration is kept up, veratroidia steadily lessens both arterial pressure and pulse-rate When the par vagum has been divided, artificial respiration being maintained, veratroidia is powerless to reduce the pulse-rate, and when the pulse-rate has been reduced by the drug in the uninjured animal, division of the par vagum is followed by an enormous rise in the number of cardiac beats per minute. These facts certainly prove that veratroidia is a powerful stimulant to the inhibitory nerves of the heart. Moreover, I have found that when the spinal cord is divided so as to paralyze the antagonists to the par vagum, a minute dose of the poison (one-thirtieth of a grain) will at once produce diastolic arrest of the heart's action, but if the pneumogastrics be now severed, and the repressive force thus taken off, the relaxed, seemingly dead viscus recommences its beat. The slow pulse of mild veratroidia-poisoning becomes rapid when a large dose of the poison is injected. Further, after a large dose division of the pneumogastrics has no effect upon pulse-rate, and the most intense galvanic current applied to the peripheral ends of the divided nerves is powerless to affect the viscus. Evidently, large doses of veratroidia paralyze the cardiac inhibitory apparatus, whilst small ones stimulate it intensely. The paralysis is certainly peripheral; whether the stimulation is centric or peripheral has not as yet been determined. When enormous doses of veratroidia are thrown directly on the heart by venous injection, they at once kill the cardiac muscle. Upon the vaso-motor nerves veratroidia in moderate toxic amounts has no demonstrable influence. Dr. F. Reigel (*Pflüger's Archiv*, 1871, p. 409) has demonstrated that the rise of arterial pressure which occurs in asphyxia is largely due to vaso-motor spasm. In viridia-poisoning asphyxia has very little influence upon the arterial pressure, because the vaso-motor centres are paralyzed; in veratroidia-poisoning the slightest intermission in the working of the bellows of the apparatus for artificial respiration is followed at once by an enormous rise of the mercury in the cardiometer, conclusive proof that the vaso-motor centres are not seriously affected. This deduction I have experimentally corroborated by galvanization of a sensitive nerve: always, unless an enormous amount of the alkaloid had been given, the rise in the arterial pressure was marked and immediate. In estimating the physiological action of veratroidia it must be borne in mind that artificial respiration was maintained during the study of the action of the drug on the heart and vaso-motor centres; that its influence on the respiratory centres is so intense as to overbalance its cardiac action, and, when the animal is left to itself, to cause death before any very decided influence has been exerted on the heart. The action of the alkaloid may, therefore, be summed up as follows: it is a powerful respiratory poison, lessening at first the frequency of the cardiac beat by stimulating the pneumogastrics, but soon losing all control over the heart, owing to the powerful influences which the induced asphyxia exerts.

The *resin* of veratrum viride, when completely deprived of the alkaloids, is nearly inert. It seems, however, to be irritating to the digestive organs, and very probably aids in the production of the vomiting occasioned by full doses of the drug.

As the action of the alkaloids of veratrum viride is very similar, and as they are the only active principles of the drug, it is very easy *a priori* to determine what the influence of the drug will be. Sufficiently numerous experiments* have been performed with the crude drug, or its preparations, to show that it acts upon the lower animals as upon man; but it is not necessary here to do more than allude to them. When taken in small doses by man, veratrum viride first reduces the force without much lessening the frequency of the pulse, but after a time the pulse falls very much in rapidity, sometimes, according to Dr. Norwood, even to thirty-five a minute.

If any exertion be made during this stage of depression, the slow pulse will be suddenly converted into an exceedingly rapid one. The slow pulse is sometimes moderately full, but is always very soft and compressible; the rapid pulse is exceedingly feeble and small, often thready, and may become imperceptible. Severe nausea and vomiting accompany or follow the reduction of the pulse-rate. That the latter is not due to gastric disturbance is, however, shown by the fact that it often precedes the stomachic symptoms, and may exist without them. Thus, Prof. Percy states that he has seen the pulse reduced to thirty per minute without nausea being induced. During the stage of depression there is always decided muscular weakness and relaxation.

After a poisonous dose the symptoms above noted are increased in intensity and become very alarming. A running, almost imperceptible pulse,—a cold, clammy skin,—intense nausea, and incessant attempts at vomiting, or retching, or hiccough,—absolute muscular prostration,—faintness,—vertigo,—loss of vision, and semi-unconsciousness, make up the group of extreme symptoms. Various observers also speak of an excruciating præcordial pain; but this I have not seen.

From these symptoms, with what has already been said in regard to the alkaloids, it follows that veratrum viride is a powerful spinal and arterial depressant, exerting little or no direct influence upon the cerebral centres. In full therapeutic doses it lowers the pulse-rate both by a direct action on the muscle (jervia) and by stimulating the inhibitory nerves (veratroidia); it diminishes the force of the heart-beat by a direct influence on the cardiac muscle (jervia), and produces a general vaso-motor paralysis (jervia) more or less complete according to the size of the dose.† Under its action the functional activity of the skin is greatly increased; but, as this is a necessary result of the profound arterial depression, there is no reason for believing that the drug has any specific influence upon the perspiratory glands. In a similar manner the excretion of bile is often indirectly increased by veratrum viride, through the severe vomiting which it induces.

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* See especially a paper by Prof. S. R. Percy, *Transactions of the American Medical Association*. Reprinted as pamphlet, 1864.

† Prof. S. R. Percy states that a dilatation of the blood-vessels of the frog's web and bat's wing can be readily seen by the microscope to follow the administration of the drug.

American hellebore undoubtedly lowers animal temperature very decidedly, but whether directly or indirectly has not been determined. I have frequently seen it reduce the bodily heat, and M. Linou (*Gazette Médicale de Strasbourg*, quoted in the *Bulletin Thérapeutique*, 1869, tome lxxvi. p. 95) states that it does so, but not so certainly as it lowers the pulse. Oulmont (*Bulletin Thérapeutique*, 1868, tome lxxiv. p. 153) asserts, as the results of his experiments, that in animals from half an hour to two hours after the administration of such doses as would produce violent symptoms without killing, the temperature fell 2°, 3°, or even 5° (C.?), and remained at this point for twenty-four hours.

THERAPEUTICS.—With our present knowledge of the physiological action of veratrum viride, it is evident that there are only two rational indications for its use, namely, to *reduce spinal action* and to *reduce arterial action.* Owing to the very great effect veratrum viride has upon the circulation, and the numerous drugs which are purer spinal depressants, it is never called for to meet the first indication, and in practice should simply be used to lessen the force of the circulation. The use of the drug in *typhoid fever* and other adynamic diseases is simply an irrational and dangerous practice, founded upon an erroneous idea of the action of the remedy.

Veratrum viride has been recommended in *mania a potu;* and in cases of irritation of the brain from drink, with strong bounding pulse, it may be of great service; but in the true *delirium tremens*, with universal adynamia, it is a thoroughly improper remedy, capable of deepening the prostration into fatal exhaustion: indeed, I have known of death occurring in this disease from its use.

When true sthenic arterial excitement is to be combated in any disease, except it be *gastritis*, veratrum viride may be employed as a prompt, thoroughly efficient, and at the same time very safe remedy,—very safe, since it is almost incapable of producing death in the robust adult, unless used with great recklessness and in repeated doses. In the early stages of *sthenic pneumonia* it offers, I believe, the best known method of reducing the pulse-rate and the temperature, and of ameliorating the disease.* It is hardly necessary to mention other individual diseases in which veratrum viride may be employed to carry out the present indication.

In *peritonitis* its tendency to cause vomiting is very much against its use, and, unless this action can be controlled, should interdict its employment. I desire, however, to call attention to its value in preventing inflammation after severe *abdominal injuries*,—indeed, after any severe injury. Thus, I am cognizant of the case of a woman whose belly was torn open by the horn of a bull; the abdominal walls were rent for about six inches, and the sigmoid flexure of the colon came out and was dragged in the dirt. It was washed, replaced, the wound sewed up, the patient restricted to low diet, and veratrum viride administered very carefully so as to keep the pulse as depressed as possible and at the same time to avoid vomiting, to aid in which opium was also given. Recovery without a bad symptom resulted.*

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* Compare Oulmont, *Bulletin Thérapeutique*, t. lxxiv. p. 146, and MM. Zuber and H Hirtz, *Ibid.*, t. lxxvi. p. 468.

As an emetic, veratrum viride should never be employed.

In chronic *cardiac diseases* it may be used in precisely those cases in which digitalis is contra-indicated,—*i.e.*, where there is excessive hypertrophy.

The contra-indications to the use of veratrum viride are cardiac weakness and the existence of general adynamia.

TOXICOLOGY.—Although veratrum viride is a remedy of great power, capable of producing the most alarming symptoms, yet I believe it to be the safest of all the cardiac depressants; certainly it is far less dangerous than aconite. Overdoses of it produce vomiting so soon and so certainly that it is somewhat doubtful whether a robust adult could be killed by a single dose of any of its officinal preparations, especially if prompt and judicious treatment were afforded. I have several times known a teaspoonful of its fluid extract to be taken; and Prof. Percy cites recoveries after the ingestion of a tumblerful of the tincture; after thirty grains of the resinoid; after two doses—a tumblerful each—of a syrup representing a pound of the root to the pint. A feeble child, eighteen months old, was killed by thirty-five drops of the tincture (*Am. Jour. Pharm.*, 1865); and a doubtful case of fatal poisoning in the adult is mentioned in *Med. Surg. Rep.*, vol. xl., 372.

I have seen the most alarming symptoms result from large medicinal doses repeated at short intervals, and have been astonished at the rapidity with which they yielded to treatment; but Dr. J. D. Blake reports (*American Medical Weekly*, No. 20, 1874) a death resulting from the administration of between three and four drops of Norwood's tincture every two hours to a babe eleven months old; and a man, convalescing from typhoid fever, was killed by a drachm of the fluid extract (*Philad. Med. Times*, xiv. 863).

In cases of poisoning, vomiting should be encouraged by large draughts of warm water until the stomach is well washed out. Then the patient should be forced to lie flat upon the back, with the head lower than the feet, and the efforts at vomiting should be restrained. If they cannot be checked, and if the prostration be severe, on no account should the patient be allowed to rise up, but must be made to vomit into a towel. A full dose of laudanum should be given by the rectum, and brandy or whisky be administered by the mouth. I have noticed that spirits will sometimes be retained only when given undiluted, and in such form will quiet the stomach at once. If the stomach refuse alcohol in any shape, the rectum should be made use of. Am-functional activity of the skin is greatly increased; but, as this is a necessary result of the profound arterial depression, there is no reason for believing that the drug has any specific influence upon the perspiratory glands. In a similar manner the excretion of bile is often indirectly increased by veratrum viride, through the severe vomiting which it induces.

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* Consult also Dr. C. S. Bishop, *American Journal of the Medical Sciences*, Oct. 1861.

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In chronic *cardiac diseases* it may be used in precisely those cases in which digitalis is contra-indicated,—*i.e.*, where there is excessive hypertrophy.

The contra-indications to the use of veratrum viride are cardiac weakness and the existence of general adynamia.

Toxicology.—Although veratrum viride is a remedy of great power, capable of producing the most alarming symptoms, yet I believe it to be the safest of all the cardiac depressants; certainly it is far less dangerous than aconite. Overdoses of it produce vomiting so soon and so certainly that it is somewhat doubtful whether a robust adult could be killed by a single dose of any of its officinal preparations, especially if prompt and judicious treatment were afforded. I have several times known a teaspoonful of its fluid extract to be taken; and Prof. Percy cites recoveries after the ingestion of a tumblerful of the tincture; after thirty grains of the resinoid; after two doses—a tumblerful each—of a syrup representing a pound of the root to the pint. A feeble child, eighteen months old, was killed by thirty-five drops of the tincture (*Am. Jour. Pharm.*, 1865); and a doubtful case of fatal poisoning in the adult is mentioned in *Med. Surg. Rep.*, vol. xl., 372.

I have seen the most alarming symptoms result from large medicinal doses repeated at short intervals, and have been astonished at the rapidity with which they yielded to treatment; but Dr. J. D. Blake reports (*American Medical Weekly*, No. 20, 1874) a death resulting from the administration of between three and four drops of Norwood's tincture every two hours to a babe eleven months old; and a man, convalescing from typhoid fever, was killed by a drachm of the fluid extract (*Philad. Med. Times*, xiv. 863).

In cases of poisoning, vomiting should be encouraged by large draughts of warm water until the stomach is well washed out. Then the patient should be forced to lie flat upon the back, with the head lower than the feet, and the efforts at vomiting should be restrained. If they cannot be checked, and if the prostration be severe, on no account should the patient be allowed to rise up, but must be made to vomit into a towel. A full dose of laudanum should be given by the rectum, and brandy or whisky be administered by the mouth. I have noticed that spirits will sometimes be retained only when given undiluted, and in such form will quiet the stomach at once. If the stomach refuse alcohol in any shape, the rectum should be made use of. Ammonia may be employed as an adjuvant to alcohol, and in extreme cases should be injected hypodermically, or even into a vein. The use of external heat is important, and mild flagellations, rubbing with coarse towels, sinapisms, etc., may be used to keep up the external capillary circulation.

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* Consult also Dr. C. S. Bishop, *American Journal of the Medical Sciences*, Oct. 1861.

ADMINISTRATION.—In administering veratrum viride, it should always be borne in mind that it will do no good in acute disease unless given in increasing doses until its physiological action is manifested. In almost all cases vomiting is to be avoided as far as possible. To do this, small quantities of the drug should be given at short intervals, and corresponding doses of laudanum (five to ten drops) should be exhibited fifteen minutes before each dose of the veratrum viride. An hour is generally the best interval between the doses. The drug should always be administered in the form of the *fluid extract* (*Extractum Veratri Viridis Fluidum*, U.S.), dose, one to three drops; or of the *tincture* (*Tinctura Veratri Viridis*,—1 to 2, U.S.), dose, three to six drops. A saturated tincture is sometimes kept in the shops under the name of *Norwood's tincture.*

VERATRUM ALBUM.—In cases of human poisoning with veratrum album the symptoms* have been—excessive vomiting, generally accompanied by severe abdominal, and often œsophageal, pain, and followed by a very severe diarrhœa; intense prostration and muscular relaxation; very pronounced reduction of the temperature and pulse, the latter being sometimes rapid and almost imperceptible in the advanced stages, and finally becoming extinct; sunken eyes, contracted, anxious countenance, a cold skin clammy with profuse perspiration, and other evidences of collapse. The mind remains clear until the last. A fatal result is very common, and, when recovery occurs, the convalescence is usually protracted.

The exact nature of the active principles of veratrum album is still in volved in doubt. Pelletier and Caventou thought that they found supergallate of veratria in it. So far as I can make out from the authorities at my command, Simon† claims that there are three alkaloids in the veratrum album,—*veratria*, *barytina*, and *jervia;* and Dr. Mossel (*Sur la Vératrine*, Thèse, Paris, 1868) certainly indicates that *sabadillia* and barytina are the same. Very recently the subject has been elaborately investigated by Chas. L. Mitchell, who finds two alkaloids in the rhizome, one of which he denominates jervia, the other *veratralbia.* The resin, when entirely freed from alkaloids, is inert. In a number of experiments made separately by Mr. Mitchell, Dr. J. R. Haynes, and myself, veratralbia proved itself a most active poison, one-tenth of a grain killing a large pigeon in four minutes, and one-twentieth of a grain a dog of fourteen pounds weight in one hour. The symptoms were nausea and vomiting, with violent purging, if the animal lived some time, salivation, muscular weakness passing into paralysis, convulsions, and death,—from failure of respiration after moderate toxic doses, from cardiac arrest after very large ones. When the fatal result had been slowly produced, intense hyperæmia of the intestinal mucous membrane was found after death. Veratralbia appears to be very closely allied in both chemical and physiological properties to veratria.

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* For cases and analysis of symptoms, see Dr. Peugnet's paper in the *New York Medical Record*, p. 121, 1872.

† I have not had access to Simon's original papers.

ARNICÆ FLORES—ARNICA FLOWERS. U.S.
ARNICÆ RADIX—ARNICA ROOT. U.S.

The flowers of the Arnica montana, a perennial composite, native of Northern Europe and Asia, and said also to be found in the Northwestern United States: The yellow flowers have about fourteen striated ligulate tridentate florets in the ray, twice as long as the disk, which consists of numerous tubular florets. The taste is bitterish and acrid. The rhizome is also employed medicinally, but is not recognized by the U. S. Pharmacopœia. Two alkaloids, *Cytisin* and *Arnicina*, are stated to have been found in the flowers. The first of these is believed to be identical with the alkaloid of the seeds of the laburnum-tree (*Cytisus Laburnum*).

Physiological Action.—Locally, arnica is stimulating, and, if in sufficient strength, decidedly irritating. Upon some skins the tincture acts even violently, rapidly developing an acute eczematous inflammation of the upper dermal layers, as manifested by hyperæmia, papules, vesicles, excoriations, crusts, and scales in regular sequence (Dr. White, *Boston Medical and Surgical Journal*, Jan. 1875).

That the influence which the drug exerts upon the general system when taken internally is very decided is certain, but the exact nature of this influence is at present unknown. Viborg (quoted by Stillé) affirms that in horses and cows it causes increased action of the heart, flow of urine, and warmth of skin, followed by very decided general depression. According to Stillé, the effects of moderate doses on man are similar to those noted as occurring in the lower animals,—namely, increase of the cardiac action, of the respiration, of the temperature of the skin, and of the perspiration and urine,—along with very decided symptoms of gastric irritation. On the other hand, it is claimed that ten drops of the tincture every three or four hours act as a decided arterial sedative (Dr. C. C. Balding, *London Lancet*, Dec. 1870). The symptoms of poisoning seem strangely to vary. Thus, in a woman, two cups of a strong infusion produced violent gastro-intestinal irritation, as shown by vomiting and choleraic diarrhœa, reduction of the pulse to 60, and finally collapse (*Bulletin Thérap.*, lxxvi.). In Barbier's case (quoted by Stillé), an infusion of eighty grains of the flowers caused giddiness, and intense muscular weakness, with spasmodic movements of the limbs. In another, not fatal, case (*London Lancet*, Nov. 1864), according to the statement of the patient, an ounce of the tincture did not produce any symptoms for eight hours, when approaching collapse, dilated, immovable pupils, with a cold, dry skin, and a feeble fluttering pulse, rapidly supervened upon an intense epigastric pain, which was increased by pressure.

In a not fatal case reported by Dr. W. A. Thorn (*Virgin. Med. Monthly*, Sept. 1883), four hours after ingestion of a fluidounce of a tincture by a young man, the pulse was 100, full and strong, the temperature normal, insensibility complete, conjunctiva anæsthetic, respirations 18 per minute; no vomiting or purging. Twelve hours later the patient became wildly delirious; the next day he suffered from burning pain in the abdomen, diarrhœa, and free diuresis.

THERAPEUTICS.—In the present state of our knowledge, the internal use of arnica is absolutely experimental. Externally it is employed to a very great extent as a stimulant application in bruises and sprains, generally in the form of *tincture* (*Tinctura Arnicæ Florum*—1 to 5, U. S.; *Tinctura Arnicæ Radicis*—1 to 10, U. S.), which may be applied pure, but sometimes as fomentations of the flowers. Its property of occasionally producing intense dermal irritation should be borne in mind. An *extract* (*Extractum Arnicæ Radicis*, U. S.) and a *fluid extract* (*Extractum Arnicæ Radicis Fluidum*, U. S.) are officinal.

VERATRINA. U.S.

This alkaloid is procured from the seeds of Veratrum sabadilla (Asagræa officinalis.* As found in commerce, it is almost always more or less impure, and occurs as a grayish-white powder of an intensely acrid taste, and producing, even in the minutest quantity, when smelled, frequently-repeated sneezing, which may continue for hours. It has when pure been considered uncrystallizable, but Merck has obtained it in rhombic prisms about half an inch in length, through the spontaneous evaporation of its alcoholic solution. It is very slightly soluble in boiling water, not at all in cold water; soluble in alcohol, freely so in ether, and still more so in dilute acids.

Veratria dissolves in concentrated sulphuric acid, with the production of a yellow color, changing in five minutes into orange, then into blood-red, and in half an hour into a splendid carmine. Masing states that this test is very faint with 0.0026 of a grain. If some bromine be dropped into the freshly-prepared sulphuric acid solution, a beautiful purple results. A more delicate test than either of those yet noted is, according to Masing, that of Trapp, which consists in warming the colorless solution of veratria in concentrated muriatic acid, when a dark-red very persistent color is produced This test is said to afford very marked proof of the presence of 0.0026 of a grain of the alkaloid, and to be especially useful when the veratria is impure.

PHYSIOLOGICAL ACTION.—Veratria is exceedingly irritating to any surface it may come in contact with, producing when given hypodermically or endermically severe pain, and when rubbed on the skin a feeling of warmth, followed by prickling, severe pain, numbness, and, if its use be persisted in, a marked redness. On the mucous membranes its action is even more decided. In the nostrils the minutest portion of it produces intense irritation, as shown by repeated sneezing and free discharge, which may be bloody. Upon the tongue a speck causes burning, with free salivation.

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* The action of *sabadalline*, the congeneric alkaloid of veratrine, has been partially studied by Dr. I. Urpav (*Montpellier Med.*, 1883, i. 274), who finds it to have only about one-twelfth the toxic power of veratrine.

When taken internally, in small doses, it produces slowing and weakening of the pulse; more freely administered, indications of gastro-intestinal irritation; and in large doses it is followed by violent vomiting, serous purging, often with intense burning in the mouth and throat, and general muscular weakness. No fatal case of poisoning is on record;* but in the experiments of Esche on himself a half-grain of the acetate produced collapse, with a pale, cold, wet skin, pinched features, a rapid, thready, irregular pulse, violent vomiting, and marked muscular tremblings. Other observers have noted more pronounced indications of convulsions; and, according to Bardsley, when absorbed through the skin, instead of purging it produces in some cases very free diuresis. On the whole, the resemblance between the symptoms as induced in man and in the lower animals is, so far as we know, complete.

The phenomena of veratria-poisoning in a mammal are violent muscular twitchings and convulsions, which are often plainly excited by external irritants, severe vomiting, generally but not always accompanied by purging, and disturbance of motion, respiration, and circulation. The pulse is at first, if the dose be not too large, quickened and strengthened, but in a very short time it becomes slower and weaker, and finally very frequent, thready, and irregular. There is early a marked loss of muscular power, even in the midst of the convulsions, and the latter may give way to the quiet of paralysis, or may continue up to death.

According to the researches of Claus (*Journal of Anatomy*, viii.) veratria in toxic doses causes first a slight fall of temperature, then a rise to about normal, and finally a fall immediately before death. Sabadillia, on the contrary, produces a rise of temperature, followed only by a partial fall, so that the bodily heat even at the moment of death is above normal.

M. Prevost (Robin's *Journal de l'Anatomie*, 1868, t. v. p. 206) has, I think, very well divided the action of veratria in poisonous doses into three stages: first, that of excitation or restlessness; second, that of convulsions; third, that of paralysis. It should, however, be understood that these may after large doses be fused into one. I have seen an animal suffer a convulsion, or perhaps merely give a convulsive shudder, and drop dead.

After death from a very large dose, the muscles are found to have lost more or less completely their irritability, so that they either do not respond, or respond very feebly, to the strongest faradaic currents. That this is due to a direct influence of the alkaloid upon them is proven by the fact, first noted by Kölliker (*Virchow's Archiv*, Bd. x. p. 257), but which I in common with other observers have experimentally confirmed, that if an artery be tied before poisoning, all the muscles supplied by that artery maintain their integrity.

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* In *St. George's Hospital Reports*, 1870, vol. v., Dr. C. Paget Blake reports a case of recovery after the ingestion of a liniment supposed to contain three grains of veratria! Intense itching of the skin was a prominent symptom.

It is evident that veratria is a muscle-poison; but it has other powers, and the subject is best studied in detail, system by system.

Central Nervous System.—Upon the cerebrum the action of veratria is not very marked. That the convulsions are not cerebral is shown by the fact, which I have frequently noted, that they are in no wise affected by division of the spinal cord. The spasms must be, therefore, either peripheral or spinal in origin. M. Prevost (Robin's *Journal de l'Anatomie*, 1868, p. 209) has found that convulsions will occur in the frog even when the spinal cord is destroyed, but that under these circumstances the convulsions are not spontaneous, but occur only when an irritation is applied to a part, and are limited to the part irritated. A fact analogous to this was noticed by Kölliker (*Virchow's Archiv*, Bd. x. p. 262, Exp. IX.): in frogs whose nerves were paralyzed by woorari, the exhibition of veratria induced phenomena similar to those just noted. These facts, however, do not prove that the convulsions in the veratrized frog are not spinal, but only show that there is a state of excitation of the muscles. But M. Prevost furnishes the following direct proof that the cord in veratria-poisoning is not affected. The hind legs of a frog were separated from the rest of the body by a very tight ligature, so placed as not to include the lumbar nerves. Some veratria was then introduced into one of the fore legs, and of course found its way into the spinal cord and the anterior portions of the body. Under these circumstances it is evident that the convulsions produced, if spinal, would affect the whole body, but if peripheral would be confined to the anterior part of the frog. It was found that the posterior legs were never affected, that whilst irritation of them caused most violent spasms in the anterior part of the body, only the normal reflex actions occurred in those muscles not reached by the poison. If this experiment be confirmed (and I see no intrinsic reason to doubt its accuracy), to Prevost belongs the credit of having proven that veratria has no action on the motor centres of the spinal cord.

There is, however, an apparent opposition between the experiments of Prevost and those of Kölliker (*Virchow's Archiv*, Bd. x. p. 261). The latter observer noted (Exp. VI.) that when the skull of the frog was opened and a ten per cent. alcoholic solution of veratria dropped on the cord, violent general tetanic convulsions were induced; also (Exp. IV.) that when one crural artery and vein of a frog were tied and the veratria solution placed in the mouth, tetanus ensued, involving the protected limb, and continuing there after it had ceased in the other members. I see no way of reconciling these experiments of Kölliker with those of Prevost except either by supposing that the latter are incorrectly observed, or, what seems more probable, that the poison in the former reached the protected parts by diffusion, although in less quantity than it did the other members: this would also explain the continuance of tetanus in the protected limb after it had ceased elsewhere.

M. Guttmann (*Reichert's Archiv für Anatomie*, 1866) is in accord with Kölliker in his experiments, for he states that, notwithstanding the artery of a limb is tied, yet spasms occur in the leg during the convulsive stage of veratria-poisoning: of course the "diffusion" theory would apply to this as well as to the experiments of Kölliker.

The only conclusion to be drawn from the evidence seems to me to be that at present it is uncertain whether veratria does or does not act upon the motor centres of the cord.

In regard to the action of the drug upon the sensitive centres of the cord, our knowledge is by no means perfect. Anæsthesia of the posterior feet was noticed in the frogs experimented upon by Prevost in the manner described; but when the circulation is cut off from the feet of a frog, loss of sensibility always ensues.

Peripheral Nervous System.—The study of the action of veratria upon the peripheral motor apparatus evidently divides itself into a study of the influence upon the muscles and the extreme nerve-endings in them, and upon the nerve-trunks.

There can be no doubt that veratria finally destroys the contractile power of the muscle itself, so that it fails to respond to any irritation whatever, and soon, becoming stiff, exhibits the acid reaction of post-mortem rigidity. Thus far all recent observers are in accord; and I have frequently witnessed the same phenomenon. Kölliker in some of his experiments (*loc. cit.*) notes that the muscle in the early stage of veratria-poisoning responded inordinately to stimuli. The study of this phenomenon has been especially made by Bezold and Hirt (*Untersuch. Physiolog. Laborat. Würzburg*, I.) by M. Prevost,* by Rossbach (*Pflüger's Archiv*, xiii. p. 617), by Marey, and Maurice Mendelssohn (*Travaux du Laborat. de M. Marey*, xiv., and *Compt.-Rend. Soc. Biolog.*, 1883, 147). When a muscle during the convulsive stage of veratria-poisoning is momentarily stimulated, instead of the usual momentary contraction a prolonged tetanic spasm results and lasts some seconds: this spasm is induced by the slightest irritation. When a nerve is irritated repeatedly within a short time, the tributary muscle loses its power of entering upon a "veratria contraction," but if left quiet for a time recovers itself. There is therefore in veratria-poisoning, preceding the stage of muscular paralysis, a stage of muscular hyper-excitability. To this are due no doubt in great part, if not altogether, the convulsions. It can scarcely be doubted that it is the result of an action not upon the nerve-endings, but upon the sarcolemma of the muscle.* That the muscular paralysis is of similar nature would seem to be proven by the rapid changes which take place in the muscle after death, and by the fact, noted by Guttmann (*Reichert's Archiv für Anatomie*, 1866, p. 498), that whilst frogs apparently dead from nerve-poisons such as atropia, strychnia, and curari often recover themselves after a period of stupor, those poisoned with veratria never do.

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* Quoted by Husemann.

When a muscle is dead, galvanization of the nerve of course elicits no response; but it is possible that a substance may be at the same time a nerve-poison and a muscle-poison. Veratria is both a muscle-poison and a nerve-poison. Kölliker denies this, but the experimental evidence brought forward by him amounts to almost nothing. Guttmann (*loc. cit.*) asserts that in his experiments, whenever irritation of a nerve failed to elicit a response, direct irritation of the muscle was always equally unavailing. Bezold and Hirt (*loc. cit.*) experimented, with a full knowledge of Guttmann's work, with small and with large doses, and evidently with great care. They found (*loc. cit.*, p. 90) that when a *small dose* is used there is at first a very marked increase in the irritability both of the nerve and of the muscle, so that, whether the current be applied directly to the muscle or indirectly through the nerve, contractions take place more readily than normal. After a time, both muscle and nerve lose their irritability, so that no contraction follows either the direct or the indirect stimulation. The process does not go on *pari passu* in the two organs. The irritability increases sooner and is sooner lost in the nerve than in the muscle, so that there is a time when galvanic irritation of the nerve fails to induce contraction, although the muscle still retains its functional power and reacts instantly to direct stimulation. Moreover, the upper or spinal end of the nerve dies first, so that at a certain stage irritation of the nerve-trunk close to its origin fails to induce contraction of the tributary muscle, although when applied lower down it elicits a response. This important observation is confirmed by Fick and Böhm (*Arbeiten aus dem Physiolog. Laborat. der Würzburger Hochschule*, 1873, p. 147), and by J. Ott (*Toxicological Studies*, Philada., 1874), and would seem to prove that veratria acts directly on the nerve-trunks. Fick, however, affirms that under these circumstances he has frequently proven the existence of the normal muscular galvanic currents in the seemingly dead nerve-trunks, and that therefore it is only the peripheral *nerve-endings* which are attacked by veratria. But it is difficult to reconcile this observation of Fick with some of those of Bezold and Hirt. At present, therefore, it must be considered undetermined whether it is the nerve-endings solely, or the whole peripheral nerves, which are affected by veratria.

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* Fick and Böhm, in the elaborate paper already referred to, believe that they prove that the prolongation of the muscular contractions in veratria-poisoning is due to a greater intensity of the chemical processes of the muscles, and not to a delay of the process of restitution. A discussion of this point would involve that of muscular physiology, and cannot be entered into here. The weak point of the argument made by Fick and Böhm may, however, be pointed out. Granting all their asserted facts, it is perfectly possible that greater intensity of the chemical processes is an *effect*, not a *cause*, of the prolonged contractions.

As already stated, the action of veratria upon the sensory centres is doubtful; its influence upon the peripheral sensitive nerves has not, that I am aware of, been carefully worked out, but the effects of its local application to the human skin seemingly show that it first strongly excites and then paralyzes them.

Circulation.—After death from a large dose of veratria, the heart is soft, dilated, full of blood, and incapable of responding to galvanism; *i.e.*, the heart-muscle is dead. According to Bezold and Hirt (*loc. cit.*), after a small dose there are quickening of the pulse and rise of the blood-pressure, which soon return to the normal condition; whilst immediate and persistent fall in the number of the heart-beats and in the arterial pressure follows a large dose. If the vagi be divided previous to the poisoning, a large dose produces a temporary increase in the pulse; and a stimulation of the distal end of the cut nerves by a current too slight to be felt in the unpoisoned animal retards very markedly the beat. From these facts it follows that in the uninjured animal, after poisoning by veratria, there is an inhibitory retardation of the pulse, and also an excitation of the peripheral ends of the vagi. That it is not merely the peripheral inhibitory apparatus which is affected was proved by injecting the alkaloid into the carotid,—*i.e.*, into the inhibitory centre,—when there happened an instantaneous and remarkable retardation of the heart-beat, which could only have been caused by excitation of the inhibitory centre. In a later stage of the poisoning the strongest faradaic currents applied to the pneumogastrics fail to affect the heart. It is, therefore, evident that veratria first exalts and then destroys the functional activity of the par vagum, as of the spinal nerves.

According to the researches of Prof. S. Ringer, veratria acts directly upon the cardiac muscle as it does upon the skeletal muscles. Each excitation causes in the veratrized frog's heart a prolonged series of inco-ordinated contractions; therefore a lessened regulation with an increased amount of force-generation (*Archives of Med.*, 1882, p. 21).

When the heart is separated from the nerve-centres by section of the par vagum and of the spinal cord, veratria produces, according to Bezold and Hirt, at first increase in the pulse and blood-pressure, secondly, lowering of both to the minimum; showing that it exerts upon the internal heart-ganglia, or upon the heart-muscle, its peculiar action of first stimulating and afterwards paralyzing functional activity.

That the poison has a similar action upon the vaso-motor centres seems probable from the facts noted by Bezold and Hirt: first, that injection into the carotid after section of the pneumogastrics causes immediate rise of the blood-pressure; second, if the mesenteric arteries have been previously bared, they can be seen to contract. This excitation is followed after a time by vaso-motor paralysis and dilatation of the vessels.

Respiration.—Bezold and Hirt conclude, from the fact that after section of the pneumogastrics even the smallest doses of veratria cause retardation of the respiration without previous increase, that the alkaloid depresses immediately the centre of respiration in the medulla, and finally kills it.

THERAPEUTIC ACTION.—The study of the physiological action of veratria shows that its rational therapeutic use must be limited. As a heart-sedative, it is much inferior to aconite and veratrum viride, for obvious reasons, and, although it has been used as such, it has not achieved much reputation. When exhibited in full doses it is very apt to give rise to exceedingly disagreeable secondary symptoms, and has no advantage over the medicines just named. Some years ago it was employed in *acute rheumatism*, having been recommended by Turnbull, Bardsley, Piedagnel, Trousseau, and others; but it is not so efficacious in this disease as other far less dangerous remedies by which it has been superseded. The same is true of its employment in *dropsy;* and I know of no condition which would justify its internal use.

Bardsley originally employed it in *neuralgia*, especially when arising from cold. He used it both internally and externally. At present it is rarely employed except as a local application. My own success with it has not been very encouraging, but others of larger experience recommend that it be rubbed over the affected nerves in *rheumatic neuralgia.*

As an external stimulant and rubefacient it is sometimes used with good effect in narcotic poisoning; also in various spinal troubles as an irritant applied to the spine, and to the skin of the paralyzed limbs, to aid in maintaining circulation; but all these indications can, I think, be better met by other means. In regard to the dose of veratria for internal use, it should be borne in mind that one-sixteenth of a grain has produced the most alarming symptoms (Taylor, *Medical Jurisprudence*, 2d edition, London, 1873).

An *ointment* (*Unguentum Veratrinæ*—1 to 26.5, U. S.) and an *oleate* (*Oleatum Veratrinæ*—1 to 50, U. S.) are officinal.

AOONITUM. U.S.

The Aconitum Napellus,* or monkshood, is a tall perennial, indigenous in Europe, and cultivated in this country for the sake of its spike of blue flowers. The leaves are three or four inches in diameter, and cut almost to the base into three to seven three-lobed, wedge-shaped divisions.

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* All of the species of the genus Aconitum are more or less poisonous, although A. Napellus is the only one officinal. For a study of the comparative strength of the various aconites, see Schroff, *Journal für Pharmacodynamik*, 1857, p. 335. He arranges them as follows, commencing with the most virulent: *A. ferox*, *A. Napellus*, with its varieties, *neomontanum*, *tauricum*, and *variabile*, *A. Cammarum*, *A. paniculatum*, *A. Anthora*. The toxic properties of the A. Anthora were very weak. *Lycoctonin* is the alkaloid of A. lycoctonum. For a physiological study of it by Dr. Ott, see *Philad. Med. Times*, vi. p. 25.

The root, which is the only officinal portion, is from three to four inches long, very tapering, about three-quarters of an inch in diameter at the base. Its taste is bitterish, acrid, and after a little while benumbing, giving origin to intense tingling of the lips and mouth. It is to be distinguished from horseradish root, with which it has been fatally confounded, by its external brown color and its absence of odor when scraped. The whole plant is active and tastes like the root.

In 1833 Geiger and Hesse discovered in aconite an alkaloid, *Aconitia*, which is undoubtedly the active principle of the drug. This alkaloid is now officinal. As prepared according to the directions of the U. S. Pharmacopœia, it is a yellowish-white powder. In commerce there are several varieties of it, made by different large manufacturers: the *German aconitia*, which is very impure, and, according to Husemann, is less active than the extract; *impure English aconitia;* and the so-called *English aconitia*, prepared by Morson and said to be chemically pure. The latter is a grayish powder.[*]

Duquesnel (*Comptes-Rendus*, vol. lxxiii., 1864) first obtained the aconitia in the form of colorless, rhombic, tabular crystals, soluble in alcohol, benzine, ether, and extremely so in chloroform, very slightly soluble in water, insoluble in glycerine.

The salts of aconite are soluble, and from their solution the alkaloid is precipitated by alkalies in an amorphous state. That aconitia is the only active principle of the root would seem to follow from the experiments of Hottot (*Journal de Physiologie*, 1864).

PHYSIOLOGICAL ACTION.—When applied to a raw surface, or to the skin, aconite, or its alkaloid aconitia, acts as a local irritant and narcotic, soon producing numbness, with tingling, which may persist for a long time. When given in sufficient dose internally, it is a violent poison, acting, so far as is known, similarly upon all animals.

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[*] In 1857, Hübschmann announced the presence in minute quantity of a second alkaloid in the root of Aconitum Napellus,—*Napellina.* Schroff[*] (*Journal für Pharmacodynamik*, i. 3) could find no essential difference between its action and that of German aconitia. T. and H. Smith, of Edinburgh, have found a third non-poisonous alkaloid, *Aconella*, which they think to be probably identical with narcotina; and Flückiger asserts that there are four alkaloids contained in the genus *Aconitum*, namely, *Aconitia*, *Pseudaconitia*,[†] *Napellina*, and *Lyctonia* (*Sydenham Year-Book*, 1869 and 1870). Recently Dr. C. A. Wright has found that there are three alkaloids in Aconitum Napellus, crystallizable aconitia, a nearly inert base, *picra aconitia*, and a third alkaloid, incapable of crystallizing or forming crystallizable salt, which is said to frequently form the bulk of commercial aconitia.

[*] From what Schroff says about the material he used in his experiments, it is evident that he had no proof that it was genuine napellina.

[†] Böhm and Ewens have physiologically studied the alkaloid of Aconitum ferox under the name of *pseudaconitia*, and found the difference between its action and that of aconitia to be one of degree, not of kind; it was the stronger of the two (*Archiv für Experim. Pathologie und Pharmak.*, Bd. i., 1873).

If the dose be large, death may be almost immediate, and, if the alkaloid be given hypodermically, may occur in less than a minute. In such cases the result is apparently due to sudden paralysis of the heart-muscle.

After moderate toxic doses, the prominent symptoms are great disturbance of the respiration, muscular weakness, vascular depression, and finally death, with or without convulsions. As I have seen the rabbit after the injection of one-sixth or one-quarter grain of Morson's pure aconitia, the animal commences to jump vertically in a very peculiar manner, and often to squeal piteously. The jumping soon grows less and less powerful, and finally is replaced by severe convulsions, during which the animal often lies prostrate on its side. In the dog, however, the muscles have remained without a quiver during all stages of the poisoning; in the horse Harley has noticed convulsions (*St. Thos. Hosp. Reports*, v.). The convulsions are an inconstant symptom, dependent upon peculiarities of the individual or species, as well as upon the amount injected. Dilatation of the pupil frequently occurs, if it be not, indeed, a constant phenomenon. There is often severe vomiting.

The symptoms which are induced by small therapeutic doses of aconite in man are reduction of the force and frequency of the circulation, a sense of muscular inertia and weakness, and a slight tingling in the extremities or in the lips. If the dose administered be large, all these symptoms are intensified; the muscular weakness is extreme; the tingling is felt all over the body; the pulse is feeble, and reduced to thirty or forty per minute; the respirations are diminished; giddiness and disordered vision may be manifested, especially when the erect posture is assumed. After three or four hours these symptoms gradually subside.

When a poisonous dose has been ingested, the first thing noticed in most cases is a burning or tingling in the throat or in the extremities, soon spreading over the whole body. The pulse rapidly falls in frequency, and in a very little time becomes exceedingly weak, intermittent, irregular, and finally imperceptible; the muscular strength is greatly reduced, and sometimes almost entirely gone; the respirations are shallow, feeble, irregular, and infrequent; the general sensibility is very much benumbed, so that marked anæsthesia of the surface is present; the skin is bedewed with a cold sweat; the countenance is anxious, sunken, livid, and the eyes are often protruded, or are even spoken of as glaring; the pupil is generally dilated, but when there are no convulsions may be contracted; gastric burning is sometimes complained of, and severe vomiting may be present, but the stomach is not rarely retentive. The intellect generally remains unaffected until very near the close, sometimes to the very moment of death.* In the collapse of the latter stages of aconite-poisoning the special senses may be lost, especially the sight. The voice is very generally extinguished. Convulsions occur in some cases, not in others: and certainly in some instances, if not always, the patient is unconscious during their continuance. Diplopia, or other disorder of vision, has been noted in some cases. Death may occur suddenly, especially *directly after some exertion* on the part of the patient, from syncope.

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* Pereira, however, states that in some recorded cases stupor has occurred.

The symptoms which aconite produces in man and in the lower animals are so entirely identical that the conclusions arrived at in regard to the latter may be accepted without reserve as applicable to the former.

Circulation.—The action of aconite upon the circulation is very decided. According to Dr. Achscharumow (*Reichert's Archiv*, 1866, p. 255), in the frog a moderate toxic dose of aconitia produces at first a reduction in the number of the heart's pulsations, then an increase in the rapidity of its action, with very evident loss of power, and finally irregular systolic movements, with very long intervening pauses ending in diastolic arrest. Dr. Rudolf Böhm and L. Wartmann (*Arbeiten aus dem Physiolog. Laborat. der Würzburger Hochschule*, 1873) have substantially confirmed these observations.

In the higher animals the exhibition of aconite in sufficient doses yields similar results. In the dog and cat (Böhm and Wartmann, and my own experiments) there is a steady sinking of the arterial pressure. In the rabbit, according to Böhm and Wartmann, the fall of pressure is preceded by a brief rise; this rise has also been noticed in the dog by Laborde and Duquesnel (*Des Aconits*, p. 130). The rate of the heart's pulsation also undergoes reduction, and there is finally diastolic arrest in dogs as in other mammals.

The method by which the aconite influences the heart is not certainly settled. According to the experiments both of Böhm and of Wartmann, it produces a gradual paralysis of the peripheral vagi, a constant increase of the intensity of a galvanic stimulation of the pneumogastric nerves being required to influence the heart as the poisoning deepens, until finally the vagi entirely refuse to transmit any inhibitory impulse.

In a single experiment, Achscharumow (p. 272) found that after section of the vagi in the early stage of aconite-poisoning there was an immediate rise both in the number of the cardiac pulsations and in the arterial pressure. From these data he argues that the slowing of the pulse during the early stage of aconite-poisoning is due to stimulation of the inhibitory centres in the medulla oblongata. Böhm and Wartmann (*loc. cit.*, p. 266) repudiate this conclusion, because, according to their experience, the phenomena of aconite-poisoning occur in the usual manner after section of the vagi, or in atropized animals. It is evident that there is no necessary contradiction in the asserted facts of these observers, as it is possible that the slowing of the pulse may be due to two immediate causes, one having its seat in the medulla oblongata, the other in the heart. Although this explanation cannot be considered proven, it is probably correct. Prof. Plugge confirms the statement of Böhm and Wartmann, that aconitine finally paralyzes the peripheral vagus, whilst Lewin agrees with Achscharumow that there is a primary rise of the pulse when aconitia is given after section of the vagi, but states that this rise is of very brief duration and is soon followed by the usual reduction (*Prager Vierteljahrs.*, Bd. cxxxi.). It is very certain that aconitia also influences directly the heart or its contained ganglia, for Achscharumow (*loc. cit.*, p. 262) has found that it acts upon the frog's heart removed from the body, and Liégeois and Hottot (*Journal de Physiologie*, p. 520, 1861) have observed the ordinary cardiac phenomena of aconite-poisoning produced by the alkaloid placed directly upon the viscus. Böhm and Wartmann have also noted that in aconite-poisoning the force of the individual beat is lessened. In the experiments of Laborde and Duquesnel, the cardiac beats were at first rendered very slow but very full and forcible, and afterwards became very rapid and very feeble (*loc. cit.*, p. 124). After death the cardiac muscle fails entirely to respond to galvanic irritation, its contractility being lost.*

Our knowledge of the action of aconitia upon the vaso-motor nerves is not complete. Achscharumow, Dr. F. B. Nunneley (*Proc. Royal Society*, p. 46, 1870), and still more recently Dr. Mackenzie, have studied with the microscope the influence of injections of aconitia upon the vessels of the frog's web, but have been unable to detect any alteration of their calibre. The first observer has also found that after division of the sympathetic in the neck, galvanization of the peripheral end produces the usual phenomena, even in the most advanced stages of aconite-poisoning. These facts indicate very strongly that *aconite does not affect the vaso-motor nerves*, and this indication is confirmed by the experiments of Böhm and Wartmann, who found that when in aconite-poisoning a galvanic current was applied to the vaso-motor centres in the medulla, an immediate rise of arterial pressure took place. As stimulation of a sensitive nerve produced at such time no rise of arterial pressure, the conclusion would appear to be logical that aconitia, whilst not affecting the efferent vaso-motor nerves or the vaso-motor centres, destroys the conducting power either of the afferent nerves or of the cord, so that in an animal under its influence no impulse can be transmitted from the periphery to the vaso-motor centres in the medulla.

Nervous System.—Such diverse experimental results have been reached by different investigators that it is very difficult to draw any positive conclusion from the evidence. Achscharumow concludes that the paralysis and loss of reflex activity induced depend upon the destruction of the conducting power of the peripheral motor nerves, because he has found that when a frog is poisoned after the abdominal aorta has been tied, reflex and voluntary activity is preserved in the hind legs long after it has been lost in the anterior portion of the body; and, at the same time, whilst the brachial nerves, as tested by galvanic stimulation, have lost their power of transmitting impulses, the protected ischiadic nerves have preserved their functional ability. The very recent experiments of Prof. P. C. Plugge (*Virchow's Archiv*, Bd. lxxxvii. p. 410) confirm these experiments of Achscharumow, showing, however, that it is the peripheral ends of the motor nerves which are affected, since, when in the frog's leg the lower portion had been protected from the poison, galvanization of the nerve-trunk a considerable distance above the point of protection caused response in the tributary muscles. This concurrence of testimony would seem to prove that aconitine *paralyzes the peripheral motor nerves.* The testimony, however, to the contrary of this is strong. Böhm and Wartmann in many experiments with Merck's aconitia found that both the nerves and muscles in poisoned animals preserve their normal excitability until death; they also determined that tying all the structures of a limb except its nerve did not prevent the usual development of paralysis when the poison was exhibited. In the elaborate research of Liégeois and Hottot, to be spoken of in detail directly, when all voluntary reflex actions were lost, the motor nerves and muscles were still found excitable. Mackenzie and A. Guïllaud (*Arch. de Physiol.*, 1875) also bear testimony to the same effect. The explanation of this conflict of testimony is not to be found, as has been suggested by C. Ewers (*Arch. Exper. Path. u. Pharm.*, i. 1873), in the use of different species of frogs, because Pluggo employed various species, nor is it in the employment of different commercial aconitias, because Plugge experimented with all the varieties, and found them to vary in power, but not in quality of action. Those observers who have found least influence upon the motor nerves acknowledge some *slight* effect, and that when aconitine is brought in contact with an exposed nerve it rapidly destroys its functional activity; also that after death in the aconitized frog the motor nerves lose their irritability more rapidly than normal (Liégeois and Hottot, Guillaud, S. Ringer and H. Murrell, Labordo and Duquesnel). Further, it has been noted that when in frogs the convulsions are very severe the motor nerves seem temporarily to lose their functional power from exhaustion (Mackenzie). Mackenzie affirms (*Practitioner*, xx. 186) that aconitia has a primary stimulant effect upon the motor nerve, and causes at first a distinct augmentation in the irritability both of nerve and of muscle.

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* Opposed to all this evidence are the extraordinary and at present inexplicable statements of Hunter Mackenzie (*Practitioner*, xxi. 109), that aconitia has no effect upon the heart, and if applied directly to it does not seriously affect its pulsations.

According to Dr. Liégeois and M. Hottot (*loc. cit.*, p. 533), in aconite-poisoning loss of sensibility occurs in the frog's legs simultaneously with or even before the disturbances of respiration, and long before the power of voluntary motion is lost, and even when the reflex activity is intact. This sensory paralysis, according to the experiments of the French investigators just quoted, first appears in the hind legs of a frog poisoned with aconitia, and has not its primary seat either in the peripheral nerves or in the spinal cord, for it was found that tying the aorta close to its abdominal bifurcation, so as to prevent access of the blood—*i.e.*, of the poison—to the posterior nerves, did not affect the development of the anæsthesia; further, that closing the artery nearer its origin in such a way as to shut off the circulation to the cord and spinal nerves, but to allow the passage of the blood to the cerebrum, did not cause sensory paralysis to come on more slowly than is normal in poisoning by aconite.

Of course it is possible for the peripheral ends of the sensory nerves to be paralyzed either at the same time that the perceptive centre is, or afterwards; and of course, the centre being paralyzed, it becomes very difficult to determine whether the periphery is or is not affected. Liégeois and Hottot assert that this paralysis of the centre occurs before any serious implication of the peripheric nerves, because after aconitic anæsthesia had been produced strychnia was able to induce tetanus; afterwards, however, the extreme peripheric nerves became affected, so that irritation of the skin in the doubly-poisoned frog would not provoke convulsions, even at a time when irritation of the trunk of a nerve would produce general reflex motor disturbance. At last galvanization of the nerve-trunk itself failed to induce response. From these facts Liégeois and Hottot deduce—very logically, I think—the conclusion that aconite induces anæsthesia by paralyzing, first, the perceptive centres; secondly, the peripheral extremities of the nerves; thirdly, the nerve-trunks themselves. The observers alluded to also confirmed this conclusion by other experiments than those already noticed. They found that although aconitia applied directly to a nerve-trunk paralyzes its sensibility, yet when the veins of a frog's leg are tied and the alkaloid injected into the artery and allowed to permeate the tissues of the leg, the skin loses its sensibility long before the nerve is affected.

In regard to motion, Liégeois and Hottot found that in a certain stage of aconite-poisoning the frog lies with his limbs extended, relaxed, and perfectly paralyzed, and yet is capable of executing vigorous voluntary movements and evinces nearly normal reflex activity. They attribute this condition of apparent but not real motor paralysis to loss of sensibility from paralysis of the perceptive centre, as the unpoisoned frog evinces the same phenomena after division of all the posterior spinal roots. After a time the reflex activity is also lost, the power of voluntary movement remaining. Liégeois and Hottot believe that this loss of reflex activity is spinal; but in their experiments upon the conjoint action of aconite and strychnia it was found that at a certain stage, when no amount of irritation of a nerve would induce convulsions, a slight direct irritation of the cord would cause violent strychnic spasms. This would seem to show that at least the earliest abolition of the reflex activity was due to paralysis of the afferent nerve-fibres.

In some particulars the researches of Liégeois and Hottot have been confirmed by the later studies of Dr. George Hunter Mackenzie (*London Practitioner*, xx. p. 100). The persistence of voluntary movement after abolition of reflex actions, which was first noted by Böhm and Wartmann, and afterwards by Liégeois and Hottot, as well as by Mackenzie, proves that at a certain stage of the poisoning, whilst the motor pathway from the brain along the anterior columns and the efferent nerves is open, either the sensory nerves or the receptive centres of the cord are paralyzed. The experiments of Liégeois and Hottot upon the joint action of aconitia and strychnia are also accordant with those of Mackenzie, for that observer found that when a nerve was protected from the poison by tying its supplying artery, irritation of it caused reflex actions when the remainder of the frog's periphery was insensible; also that there is a stage of poisoning in which irritation of the extreme peripheral nerves fails to induce reflex movements, although such movements are called out by irritation of the sensory nerve-trunk; later irritation of the trunk was powerless, whilst irritation of the posterior columns of the cord still produced wide-spread movements. It must therefore be considered proven that aconite *paralyzes the sensory nerves, commencing at their peripheral endings*, and that the loss of reflex activity is due, at least in great part, to such cause.

The apparent contradiction between those investigators who have reached the conclusion just given and those who have found the motor nerves especially affected (see p. 178) can, it seems to me, be reconciled only by the theory that *aconitine acts upon the peripheral ends both of sensory and of motor nerves;* which nerve is most severely affected may possibly depend upon the size of the dose employed, or, more probably, upon the physical condition of the frog. The excessive numbness and tingling of the local and general action of aconitine upon man indicate that in *the higher animals it especially affects* the sensory nerve endings.*

The supposed action of aconitia upon a higher perceptive centre is at present very doubtful. S. Ringer and R. Murrell (*Journal of Physiology*, i., Nos. 4 and 5) deny the accuracy of the delicate experiments of Liégeois and Hottot. Curiously enough, Drs. Ringer and Murrell, whilst doubting the experiments of Liégeois and Hottot, accept the conclusions founded upon these asserted erroneous experiments, seemingly because they themselves have found that aconitia causes abolition of reflex action more rapidly in brainless than in normal frogs. It is evident that even if this were invariably the case it would in no way prove the conclusions of Liégeois and Hottot. Further, the experiments on brainless frogs were only three in number, and it is perfectly possible that the rapid reflex palsy was simply the result of batrachian idiosyncrasies. The only safe conclusion on the evidence is that the evidence does not warrant any conclusion.

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* Laborde and Duquesnel (*Des Aconits*, Paris, 1883, p. 103) believe that they have demonstrated that aconitine does not act upon the sensory nerves. Their chief experiments consisted in tying the vessels of a dog's leg in such a way that no blood could return to the body, and injecting the alkaloid into the limb, after cutting the nerve. Under these circumstances they found galvanization of the centric end of the nerve continued to elicit response. At most such experiments prove nothing as to the action of the poison upon the *peripheral nerve endings*. Moreover, it remains uncertain whether the aconitine really came in contact with the divided nerve, as all circulation in the limb must have been arrested.

It is evident that we have not exact knowledge as to how aconite affects the nerve-centres,* but the nervous phenomena of aconite-poisoning seem to me explainable by the action of the drug upon the sensitive and motor nerves.

Respiration.—The action of aconite upon the respiration is very decided. In mammals the respirations, under the influence of the drug, are slow, with a prolonged expiration following immediately upon the inspiration. After the expiration there is a long pause. The whole breathing cycle resembles very much that occurring after section of the vagi; and, like the alteration in breathing after this section, seems to be due at least in part to paralysis of sensory or afferent fibres. The known influence of aconite upon the peripheral afferent nerves in general suggests that the poison disturbs respiration by paralyzing the peripheral afferent fibres of the vagi. Mackenzie states that in the aconitized animal section of the vagi produces no effect on the respiration; and Böhm and Wartmann (p. 127) affirm that aconite produces its usual effect after division of the nerves. It is plain that even if the aconite does paralyze the peripheral afferent vagi, it must also act upon the respiratory centres, since arrest of respiration could not be caused by afferent palsy. As the arrest occurs in the frog before the motor nerves are affected by the poison, Liégeois and Hottot believe that the disturbance is centric; and I think there can be no doubt that *aconite is a direct depressant and paralysant of the respiratory centres.*†

Close studies of the action of aconite upon the temperature in health are wanting. Achscharumow found in fatal poisoning a fall of about 3° C.*

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* Experiments by Mackenzie on frogs have yielded apparently contrary results to those of Böhm and Wartmann as to the effect of removal of the influence of Setschenow's centre upon the cord in aconitized frogs. The difference probably depends upon difference in the doses employed. Böhm and Wartmann distinctly state that when minute doses of aconitia are employed there is a primary period of excitement of the spinal centres. Mackenzie has found that the convulsions which are so severe in frogs after small quantities of aconite are chiefly of spinal origin, but that the peripheral motor apparatus shares the stimulation with the spinal motor tract. M. Guillaud (*loc. cit.*, p. 769) also affirms this primary stimulant spinal action. If it exist at all in mammals, it is in them completely masked. The convulsions seen in aconite-poisoning in some mammals are cerebral, not spinal, as I have experimentally determined that they do not occur in those portions of the body separated by spinal section from cerebral influence.

As Böhm and Wartmann found that the reflex activity was lost more rapidly than the power of voluntary movement, and that no increase of reflex activity occurs in the aconitized frog when the cord is cut so as to release it from the influence of Setschenow's reflex inhibitory centres, they draw the conclusion that the aconitia first depresses the reflex activity of the sensitive spinal centres and afterwards that of the motor spinal centres, until the cord is completely paralyzed.

† Laborde and Duquesnel affirm that after very large doses of aconitine the animal dies of spasm of the glottis and diaphragm, because they have noticed, especially in the young animal, drawing in or constriction of the lower chest during life, and *sub-pleural ecchymoses* after death. These are, however, the marks of paralysis of the glottis from palsy of the recurrent laryngeal nerve.

THERAPEUTICS.—Our knowledge of the physiological action of aconite, although imperfect, is sufficient to show that there are only two or three indications to meet which the drug may be used.

The first of these is to *lower arterial action*, and often, with it, excess of temperature. For this purpose aconite is very valuable. I have never used it in those cases, such as *pneumonia*, in which a sudden and very powerful effect is desired, simply because veratrum viride seemed to me safer, more readily controlled, and equally effective. Aconite may, however, be used with very good results in these cases, and especially in such diseases as *peritonitis*, in which it is very important to avoid vomiting. My own experience with it has been in *fevers* of a sthenic type not dependent upon so deep-seated a cause (as an example may be mentioned the febrile movements of severe, acute *muscular rheumatism*), and in the *ephemera* or *irritative fevers* of childhood: in such cases its influence for good is often very decided. In the early stages of *scarlet fever* and other *exanthemata*, when not decidedly adynamic in type, it is very useful. In the reflex fever which sometimes follows the passage of the catheter or bougie (the so-called *urethral fever*) it is very efficient.†

In some cases of *hypertrophy of the heart*, when the valves are perfect, or when, the valves being diseased, the *hypertrophy* is greater than is necessary, aconite is of use to control cardiac excitement. When, however, there is dilatation of the heart or any degeneration of the heart-muscle, it is an exceedingly dangerous remedy, and is also at all times to be avoided if the hypertrophy be not excessive.

A second indication, which aconite might be used to fulfil, is to *allay spasm*. As, however, its influence upon the motor centres and nerves is much less than upon the sensitive centres and nerves and upon the heart, the indication is better met by other remedies.

A third indication, which it would seem from its known physiological action that aconite should meet, is to *relieve over-excitation of the sensitive*

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* MM. Gréhaul and Duquesnel (*L'Union Pharmaceutique*, Aug. 1871) have communicated to the French Academy some experiments upon frogs with *crystallized aconitia*, whose results are so strikingly different from those of other experimenters as to indicate the existence of some fallacy; possibly the alkaloid used by them was not the same as the amorphous aconitia. They found in the frog, after small doses ($\frac{1}{20}$ milligramme) of their alkaloid, that the heart continued to beat steadily and regularly after all power of spontaneous or reflex movement had been lost, that sensation was preserved as long as any power of motion existed, and that the motor nerve-trunks were paralyzed. After large doses (one milligramme) they observed sudden arrest of the heart's action. These results are, however, entirely discordant with the later ones of Laborde and Duquesnel.

† The following formula affords an excellent combination: ℞ Tr. aconit. rad., gtt. i; Sp. ether. nitrosi, f ʒii; Mist. potass. citrat., q. s. ad f ℥i. S.—Dessertspoonful every two hours for a child three years old.

nerves. Clinical experience has confirmed this. As long ago as 1834, Dr. Turnbull (*On the Preparations and Medical Employment of Aconitina by the Endermic Method*, London, 1834,—*On the Medical Properties of the Natural Order Ranunculaceæ*, London, 1835) called attention to the use of the alkaloid in *neuralgia;* and his estimate of its value has been confirmed by Dr. A. Fleming (*An Inquiry into the Physiological and Medicinal Properties of the Aconitum Napellus*, Edinburgh, 1845) and by other observers.

In cases of *rheumatic neuralgia* dependent upon an acute exposure to cold and attended with more or less febrile disturbance, in combination with other suitable remedies aconite is often of great service. In *chronic neuralgia*, associated as it always is with a lowered systemic tone, the remedy is less efficient; yet in some cases it seems to give relief. Owing to its very marked local benumbing influence, applied to the painful part it is sometimes very useful. In my own experience, this local use of it has, however, very seldom been effective when, as in *migraine*, the pain is of centric rather than of peripheral origin.

Given in full doses in the reflex *vomiting* of *pregnancy*, aconite is often advantageous, acting probably by benumbing the sensory reflex centres, or possibly the afferent peripheral nerves. I have noticed that relief lasts only so long as decided constitutional effects from the drug are apparent.

TOXICOLOGY.—Aconite is an exceedingly powerful poison, one-twelfth of a grain of the crystallized alkaloid being, according to Duquesnel, sufficient to kill a rabbit in a short time. Five grains of an extract and eighty minims of a tincture are said to have caused death (Reichert, *Philad. Med. Times*, Nov. 1881, p. 105). The symptoms usually come on in a very few minutes. In the shortest case I have met with, death occurred in thirty minutes. The average time of death (Reichert, *loc. cit.*) is three and a third hours: the longest recorded case being five and a half hours.

The *aconitines* of commerce vary inordinately in strength, so that whilst one-sixteenth of a grain (prepared by Petit,* of Paris) caused the death of Dr. Carl Meyer in five hours, several grains of the impure article, so largely sold, have been recovered from. The symptoms have been in general those of aconite poison, but excessively violent pains and convulsions have been very marked features of some of the cases. (For a very valuable general discussion of aconitine-poisoning, by Dr. Thomas Stevenson, see *Guy's Hospital Reports*, 3d series, xxvi. 308.)

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* In the researches of Anrep, Duquesnel's crystallized aconitia was nearly twice as strong as a German alkaloid used by him, which in turn was much stronger than an English article. Plugge found Petit's aconitia eight times as strong as that of E. Merc. Langgard found an alkaloid prepared from *A. japanicum* exceedingly powerful. The best discussions of the relative strength of these alkaloids I know of may be found in *Schmidt's Jahrb.*, Bd. ccii. 124, and in *Des Aconits*, by Dr. J. V. Laborde and H. Duquesnel, Paris 1883.

The peculiar tingling is the only diagnostic symptom, but it is very characteristic. The first indication for treatment is to evacuate the stomach and wash it out well with the stomach-pump. Alcoholic stimulants should be freely administered, hot and concentrated, and alcohol, ether, and digitalis be given hypodermically; the injection of ammonia into the veins may be practised. Great care should be used to keep the patient absolutely quiet, upon the back, with the feet a little higher than the head. Laborde and Duquesnel affirm that in the lower animals death after a usually fatal dose of aconitine can be prevented by artificial respiration, and in a case of human poisoning, if the heart's action were at all sustained, and the respiration failing, Sylvester's method might be resorted to.

It was discovered by Dr. J. Milner Fothergill (*Digitalis*, London, 1871, p. 6) that in the aconitized frog, even when cardiac action has ceased, digitalis has power to recall the systolic movements. More recently this antagonistic action of aconite and digitalis upon the frog's heart has been abundantly proven by various experimentalists. Clinical experience, although still limited in extent, strongly corroborates the experimental evidence of the value of digitalis. Successful cases may be found in *British Med. Journ.*, Dec. 11, 1872 (f℥i Fleming's tincture, Tr. Digitalis ♏x, hypodermically); *Boston Med. and Surg. Journ.*, Oct. 1879, 544 (fʒiii Tr. Aconit. Rad., Tr. Digitalis ♏lx, hypodermically); *Indian Med. Gazette*, xvii. 323 (Aconitum ferox root 48 grains, Tr. Digitalis ♏xxv, hypodermically, and fʒi by mouth); *Philad. Med. Times*, xiii. 328 (a decoction of aconite, amount unknown, Tr. Digitalis in drachm and half-drachm doses, by mouth). In a successful case treated by Dr. Elliot (*Lancet*, 1878, ii. 917) nitrite of amyl freely inhaled seemed to do great good: a fluidounce of a concentrated aconite liniment was thought to have been taken. Ammonia injections were unsuccessful in a case reported in the *Australian Med. Jour.*, 1879, i. 283.

ADMINISTRATION.—Aconite is never used in substance. The dose of the *tincture of aconite* (*Tinctura Aconiti*—1 to 2.5, U. S.) is one to five drops, repeated every one to three hours *pro re nata*, its effects being always watched. Fleming's tincture is a stronger preparation (℥xss to Oj).

The dose of the *extract* (*Extractum Aconiti*, U. S.) is one-quarter to three-quarters of a grain; of the *abstract* (*Abstractum Aconiti*, U. S.), one grain; of the *fluid extract* (*Extractum Aconiti Fluidum*, U. S.), one to two minims. The tincture or the fluid extract of aconite is very frequently added to stimulating and anodyne liniments.

Aconitine is not officinal, and, on account of its intense activity, should not be given internally; even its external use requires care. The ointment may be of the strength of two grains to the drachm: a two per cent. solution of the oleate of aconitine in oil has been highly commended as a local application in neuralgia.

ACIDUM HYDROCYANICUM—HYDROCYANIC ACID.

Pure hydrocyanic acid is a colorless, transparent, volatile, inflammable liquid, giving rise to giddiness and headache when smelled, and having, it is said, a burning bitter taste. So poisonous is it that when inhaled it causes death, and it must be handled with the greatest caution: smelling and tasting of it are excessively dangerous proceedings. It is indeed an imperative rule that no one should experiment with anhydrous prussic acid alone, or under any circumstances in summer, or in a warm room, or in an apartment whose open windows and doors do not admit of a free draft of air. The chemist Scheele, the discoverer of prussic acid, is believed to have been killed by the inhalation of the fumes of this material, whose poisonous properties were first pointed out by the Berlin apothecary Schrader in 1803. The anhydrous acid is soluble in water and alcohol, but is never kept in the shops, and is not officinal.

Hydrocyanic acid of common medical parlance is the officinal *Dilute Hydrocyanic Acid* (ACIDUM HYDROCYANICUM DILUTUM, U. S.), a colorless, watery solution, containing two per cent. of the anhydrous acid. Its odor and taste are the familiar ones of peach-kernels and bitter almonds; its reaction is faintly acid. According to the directions of the U. S. Pharmacopœia, it is prepared by distilling a mixture of ferrocyanide of potassium, sulphuric acid, and water, or by precipitating cyanide of silver from its watery solution with muriatic acid. With solution of nitrate of silver added in slight excess, one hundred grains of it produce a white precipitate, which, when washed with water until the washings are tasteless, and dried at a temperature not exceeding 212°, weighs ten grains, and is wholly soluble in boiling nitric acid.

The precipitate in this case is the cyanide of silver, and the amount afforded shows that the liquid contains the officinal percentage of anhydrous prussic acid.

As hydrocyanic acid has a great tendency to undergo spontaneous decomposition, especially under the influence of light, it should be kept in well-stopped, dark-colored bottles.

PHYSIOLOGICAL ACTION.—In warm-blooded animals, poisoning by hydrocyanic acid divides itself naturally into the acute and the subacute; death occurring in the first in at furthest ten minutes, in the second not at all, or else only after the lapse of a longer time than that noted. After a full dose of the strong anhydrous acid, the animal gasps once or twice, and then instantly falls in a tetanic or clonic convulsion, or else drops motionless and powerless upon its side. In either case, at once the signs of asphyxia manifest themselves, and grow more and more intense, until they end in total arrest of respiration. The heart beats irregularly, often at first slowly and strongly, with intervals of suspension of movement, but always becoming weaker and more rapid in its action, until, after the breathing has ceased, its efforts gradually die away. If the dose has been enormous, the heart and lungs may stop acting at once;

otherwise the cardiac pulsations may continue some minutes after the arrest of respiration. Ordinarily, three distinct stages are apparent: a first, very brief one, of difficult respiration, slow cardiac action, and disturbed cerebration; a second, convulsive stage, with dilated pupils, violent convulsions, unconsciousness, loud cries, vomiting, often spasmodic urination and defecation, erections, etc.; a third period, of asphyxia, collapse, and paralysis, sometimes interrupted by partial or even general spasms.

The slow form of the poisoning follows the exhibition of the poison in an amount just sufficient to kill. After the ingestion of such a dose, no phenomena are offered for some seconds; then the breathing becomes labored, and the pulse slow and full. The animal perhaps cries out, and muscular tremblings invade the whole body, to give place, in a very short time, to clonic and tonic convulsions, which continue at intervals until the third stage, that of collapse, is developed. The convulsions are less violent and less frequent than those of the acute poisoning; all the symptoms noted as occurring during the second stage of rapid cases are present in the corresponding period of the subacute poisoning, although less violent and less intense in their manifestations. When the third stage is developed, the anæsthesia is marked, affecting first the hind legs, but finally spreading to all parts of the body, and even being complete in the widely-dilated pupil. Death finally results from failure of respiration. Recovery may occur even after the conjunctiva has lost its sensibility; the return to life by a subsidence of the symptoms is usually rapid, so that generally in from one-half to three-quarters of an hour the animal will be eating as though nothing had happened. Coullon, however, noted persistence of paralysis, in some cases, for days.

In man, prussic acid produces results closely parallel with those which it causes in the lower animals. The symptoms come on suddenly. In a moment or two the individual falls to the ground insensible and convulsed, the respirations arrested or occurring at long intervals, the eyes salient, the pupil dilated, the mouth covered with bloody froth. If the dose be sufficiently large, death may occur in three or four minutes; if less have been taken, deep insensibility, tetanic or clonic convulsions, dilated pupils, a bloated countenance, cyanosed surface, set jaws, and irregular respiration, constitute the chief symptoms. The breathing is mostly convulsive, with deep, forcible expirations, but in some cases it has been stertorous. Death results from asphyxia. After small toxic but not lethal doses of prussic acid, giddiness, lightness of the head, nausea, a quick pulse, and muscular weakness, are the chief symptoms.

Action on Blood.—As early as 1814, Dr. F. B. Vietz (*Medicin. Jahrb. d. k. k. Oesterreich. Staates*, Bd. ii., 1814) called attention to the change of color that occurs in the venous blood of animals poisoned with prussic acid; and his observations have been confirmed by E. L. Schubarth (*Horn's Archiv f. Med. Erfahrung*, Berlin, 1824), by J. F. Sobernheim (*Handbuch der Prakt. Toxicologie*, Berlin, 1838), and by Dr. Coze (*Gazette Médicale* *de Paris*, 1849). In his *Leçons sur les Substances toxiques*, p. 193 (Paris, 1857), Claude Bernard reaffirms the occurrence of these changes, and further states that if the animal die suddenly the blood in the veins and right heart is found of a bright arterial hue at the post-mortem. Notwithstanding all this testimony, J. R. Bischoff (*Ueber Vergiftungen nebst einigen Versuchen an Thieren, welche mit Blausäure, Cyankalium und Arsenik angestellt wurden*, Wien, 1844) and numerous other observers have found that after death from prussic acid, either in man or other mammals, nothing but dark venous blood exists in the body. Of the correctness of this observation there can be no doubt.

Prof. W. Preyer (*Die Blausäure*, Bonn, 1870) has afforded by his experiments an explanation of these apparently contradictory facts. He found that directly after the exhibition of prussic acid to a mammal the blood becomes, even in the veins and in the right heart, of a bright arterial hue, but that after a time this color darkens into the blue of venous blood, and finally, even in the arteries and in the left ventricle, only blood of such character is to be found. Dr. Carl Gaethgens (Hoppe-Seyler's *Medicinisch-chemische Untersuchungen*, Berlin, 1866, p. 324) has, in a number of experiments, confirmed this, so it must be accepted as a fact. When an animal dies suddenly from cardiac paralysis, during the first stage of poisoning, this excessive arterialization may be found after death, as mentioned by Claude Bernard; and, as Preyer first noticed, in cold-blooded animals the bright color persists for many hours. By spectroscopic examination Prof. Preyer (*loc. cit.*, p. 95) found that the dark blood of prussic acid poisoning is absolutely or almost free from oxygen, showing only the absorption bands of deoxidized hæmoglobin, whilst Gaethgens (*loc. cit.*, p. 328) has discovered that the red venous blood of the first stage of the poisoning shows very clearly the absorption bands of oxyhæmoglobin. The first question which arises at this juncture is as to the causes of these changes of the blood, its primary excessive arterialization, its secondary excessive carbonization. Prof. Hoppe-Seyler affirms (*Medicinisch-chemische Untersuchungen*, p. 140, Berlin, 1867) that the appearance of red blood in the veins is because the red blood-corpuscles have been so acted upon by the poison as to have lost their ability of yielding up their oxygen in the capillaries. Dr. Carl Gaethgens (*Ibid.*, p. 325) has by an elaborate series of experiments shown that in the first stage of prussic acid poisoning much less than the normal amount both of carbonic acid and of exhaled oxygen is eliminated. The lessened exhalation of oxygen probably depends simply upon a lessened inhalation of oxygen, owing to the disordered respiration. That the lessened excretion of carbonic acid is not due to the same cause, however, is shown by the fact, determined by Gaethgens (*loc. cit.*, p. 347), that the percentage of the acid in the expired air is less than normal, whilst that of oxygen is greater than normal. It is evident that if the lessened excretion of carbonic acid were produced by the entrance into the lungs of an amount of air insufficient for the wants of the system, the expired air would contain more than its normal proportion of carbonic acid and less than its normal amount of oxygen. The observed phenomena seem to me to prove that during the first stage of prussic acid poisoning oxidation is arrested. They do not demonstrate, however, that the arrest is due to a direct action of the poison upon the blood-corpuscles. The probabilities of such occurrence are rendered very slight by the investigations of Gaethgens himself, for he found that when the experiments were prolonged from seventeen to forty-four minutes, much more than the normal amount of carbonic acid was exhaled, a fact in accord with the excessive carbonization of the blood known to take place in protracted hydrocyanic acid poisoning. As it seems incredible that a substance should one minute paralyze the ozonizing power of the blood-corpuscles and the next minute increase it, it is very improbable that the super-arterialization of the blood in the first stage of prussic acid poisoning is due to a direct action of the poison upon the red disk.

Preyer has proven (*loc. cit.*, p. 85) that when to blood at the temperature of the body hydrocyanic acid is added, the spectrum after a time is altered and new absorption bands appear. These bands are due to the formation of a new compound by the union of the hæmoglobin and the hydrocyanic acid. This substance, *cyanohæmoglobin*, was first discovered by Hoppe-Seyler (*Virchow's Archiv*, Bd. xxxviii. p. 475), and has no ozonizing power whatever; to its formation, no doubt, is owing the loss of ozonizing power by blood to which hydrocyanic acid is added outside of the body, a phenomenon pointed out by Schönbein* (*Schmidt's Jahrbücher*, Bd. cxl., 1868, p. 161), and indicated even earlier by the researches of Prof. Harley (*London Philosophical Transactions*, 1865, p. 706).† The latter observer found that the blood taken out of the veins of a subject forty-eight hours after death from prussic acid poisoning, and thoroughly arterialized by shaking with air, and then allowed to stand, yielded gas containing 19.56 parts of oxygen, 80.44 parts of nitrogen, and 0.00 parts of carbonic acid.

These facts at first sight seem to prove the theory of Hoppe-Seyler, to which indeed they no doubt gave origin. Preyer has shown (*loc. cit.*, p. 95), however, that the dark blood of prussic acid poisoning has not lost its power of oxidization, for on being shaken with the air it assumes the red arterial hue; and Drs. Lecorché and Meuriot (*Archives Générales*, t. xi., 6e série, p. 539) have determined that artificial respiration will produce the same result in the poisoned animal. Moreover, the spectroscope shows plainly that the hæmoglobin exists in the blood either in its pure state (Preyer, *loc. cit.*, p. 95), or else as oxyhæmoglobin (W. Laschkewitsch, *Reichert's Archiv*, p. 652, 1868; Hiller and Wagner, *Lancet*, 1877, ii. p. 933), and that no cyanohæmoglobin is present. The reaction between hydrocyanic and hæmoglobin is one requiring some time, and evidently does not occur in poisoning. On the whole, therefore, I think that the chemical evidence clearly shows the falsity of the theory that prussic acid acts in the body directly upon the red blood-corpuscles.

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* In the same memoir Schönbein calls attention to the fact that prussic acid destroys also the ozonizing power of living vegetables, such as roots, fungi, etc.

† According to Dr. E. Ray Lankester (*Pflüger's Archiv*, 1869, p. 492), when blood is shaken with cyanogen gas, and allowed to stand for two or three hours, the spectrum-changes are exactly the same as after similar treatment of blood with CO. The compound of cyanogen and hæmatin (Cy,Hb) offers not only the identical spectrum of CO,Hb, but, like the latter, is unaffected by reducing agents. After the blood stands awhile, according to Dr. E. Ray Lankester, the spectrum of hydrocyanic acid (H,CN) becomes visible in it, and the Cy,Hb undergoes conversion into the cyanohæmoglobin (Cy,Hb) of Hoppe-Seyler.

Any one desirous of investigating this subject more deeply than can be done in a work like the present should consult especially the papers by Hoppe-Seyler, *Virchow's Archiv*, Bd. xxxviii., and scattered through the *Medicinisch-chemische Untersuchungen*; by Harley, *London Philosophical Transactions*, 1865, p. 706; and by Preyer, *Pflüger's Archiv*, 1868, p. 395.

Preyer (*loc. cit.*, zweiter Theil, p. 88) has shown that the excessive oxygenation and the subsequent excessive carbonization of the blood are not peculiar to hydrocyanic acid poisoning, but are equally present after the exhibition of sulphuretted hydrogen, and even after mechanical closure of the mouth and nose. It is possible that an increased arterial pressure, an increased rapidity of circulation, may cause the blood to pass too quickly through the capillaries to allow time for the usual changes; but this has not been proven, and at present it must be acknowledged that we are ignorant as to the immediate cause of the blood-changes in these cases.

It is possible, although scarcely probable, that the changes in the color of the blood are due to alteration in the form of the corpuscles. According to Ernst Geinitz (*Pflüger's Archiv für d. gesammte Physiologie*, Bd. iii., 1870, p. 46), outside of the body prussic acid produces in the blood-corpuscles of the frog, first, a shortening of the long and a lengthening of the short diameter, and consequently a rounded form, then granulations, and, finally, a solution and setting free of the nucleus. In frogs poisoned with prussic acid a rounded form of the corpuscles was commonly exhibited, and sometimes granulations were present. M. Geinitz also found that the red disks of mammalian blood, exposed to the vapor of hydrocyanic acid in the moist chamber of Stricker, become first somewhat asymmetrical, then mulberry-shaped, and finally undergo molecular destruction. In poisoning of mammals, according to the same investigator, the granular blood-corpuscles are commonly met with. Preyer (*loc. cit.*, zweiter Theil, p. 91) confirms the observation of Geinitz so far as the action of the poison upon drawn blood is concerned, but both he and Hünefeld (*Der Chemismus in der thierischen Organisation*, Leipsic, 1840) assert that immediately after death from prussic acid the corpuscles offer their usual characters.

Whatever may be the cause of the changes in the blood, the experiments of Lewisson (*Reichert's Archiv*, 1870, p. 352) would appear to prove that the action of the poison on the nervous system is a direct one, and not due to these changes in the vital fluid, for the observer mentioned found that prussic acid acted upon the bloodless "salt frog" as upon the normal batrachian.

Action on the Heart.—The action of hydrocyanic acid upon the *heart* varies according to the dose. In sufficient amount and concentration it produces instantaneous diastolic arrest, which is either permanent or re-occurs after a few slow feeble beats (Preyer, *loc. cit.*, p. 52, and Drs. Lecorché and Meuriot, *Archives Générales*, t. xi., 6e série, p. 543). As early as 1826, Krimer found that prussic acid placed directly upon the heart of the frog produces arrest of its beat and loss of its muscular irritability. Preyer has confirmed this, and it would seem to be proven that the cardiac arrest spoken of above is due to a direct action upon the heart-muscle or its contained ganglia, yet that after cardiac death from prussic acid the heart responds to galvanism.

The cardiac results of the exhibition of small non-toxic doses are, according to Preyer, simply slowing of the heart's action.

Preyer and Laschkewitsch agree as to the action of large, but not enormous, doses. At first there is a sudden prolonged diastolic arrest of the heart, followed by an augmentation in the rapidity of the cardiac action, and after this a diminution of the rate,—to the normal number in cases of recovery, to cardiac stand-still in cases of death. Both Preyer* and Laschkewitsch (*Reichert's Archiv für Anatomie*, 1868, p. 653) found that after section of the vagi the primary diastolic arrest of the heart did not occur. The recent investigations of Jos. Lazarski confirm the statements of Preyer as to the action upon the vagus. A complete inhibitory arrest of the heart was rarely achieved, yet slowing of the pulse was constantly produced by moderate doses of the poison in the normal animal, but was prevented by previous section of the vagi, and was removed, when present, by division of the inhibitory nerves (*Wien. Med. Jahrb.*, 1881, 141). It would seem, therefore, proven that small doses of prussic acid *stimulate the cardiac inhibitory nervous system.* Böhm and Knie noted that large doses of the acid caused slowing of the pulse whether the vagi were cut or not (*Archiv für Exper. Path. und Therap.*, ii. 137), and in this have been confirmed by Lazarski. This slowing would seem to be due to a direct action upon the muscle, as Lazarski found that the cardiac accelerator nerves are not paralyzed.

Moderate doses of prussic acid seem to produce a primary very brief but great rise in the arterial pressure, followed by a fall to or below the normal. This primary rise has been noticed by Böhm and Knie, by Wahl (*De Vi et Effectu Hydrocyanato ad Curationem Attrib.*, Bonn, 1865), by Rossbach and Papitzky (*Centralb. Med. Wissens.*, 1877, p. 640), and by Lazarski. I does not seem to be altogether the result of the asphyxia produced by the acid, as it is recorded by Böhm and Knie (*loc. cit.*, p. 146) as occurring when artificial respiration was used, and Lazarski has confirmed this. All observers agree that it is followed, if the dose of the poison has been large enough, by a profound sinking of the arterial pressure. Lazarski found that galvanization of a sensitive nerve has no effect at this time upon the blood-pressure, so that we must consider that hydrocyanic acid *primarily stimulates very briefly the vaso-motor system directly or indirectly, and afterwards paralyzes it.*

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* Preyer (*loc. cit.*, p. 93) has also noted the same absence in curarized animals poisoned by hydrocyanic acid.

Action on Respiration.—According to Preyer (*loc. cit.*, pp. 17, 18, 19), during all three stages of hydrocyanic acid poisoning the respirations are lessened in frequency, and during the latter moments of life the efforts at breathing are very distant, and finally cease before the arrest of cardiac movements. The observer just mentioned found that, after division of the vagi, normally lethal doses did not kill, and that when death was brought about by the exhibition of larger doses it was by cardiac arrest. From this he deduces the conclusion that the prime respiratory action of the poison is upon the peripheral ends of the vagi. Dr. Preyer's experiments have been partially confirmed by Drs. Lecorché and Meuriot (*loc. cit.*, p. 538); but Boehm and Knie (*Archiv für Exper. Path. und Therap.*, Bd. ii. p. 135) have in a series of experiments found that section of the vagus has no influence upon the respiratory action of the poison, and in this have been confirmed by Jos. Lazarski (*loc. cit.*). Even if investigations had proven the correctness of Preyer's experiments, his conclusion could not be considered established, because we know so imperfectly the normal relations of the pneumogastrics to respiration. Moreover, Prof. Joseph Jones (*New York Medical Record*, vol. ii. p. 459) found that whilst to kill an alligator by the administration of prussic acid required a considerable length of time, its application to the medulla produced within one minute a most powerful expiration, ending in permanent contraction of the muscles of respiration and collapse of the lung. We must, it seems to me, at present consider that the respiratory phenomena of prussic acid poisoning are due to an influence exerted directly upon the respiratory centre.

Action on Muscles and Nerves and Nerve-centres.—Dr. Kölliker (*Virchow's Archiv*, Bd. x. p. 272) has found that in frogs dead of prussic acid poisoning both the nerve-trunks and the muscles are unexcitable, or that the muscles respond very feebly to direct stimulation. This is in accord with the experiments of Stannius (*Archiv für Anatomie*, 1858, p. 95), who found that when strychnia and prussic acid were given together, the convulsions normally produced by the former poison were altogether absent, or present only in a slight degree. In order to determine whether the nerves are or are not primarily affected, Kölliker experimented by tying the vessels of the thigh, then dividing just below this point all the tissues except the nerve, and administering prussic acid by the mouth. In a number of such experiments he found that always the nerve and muscles below the point of section retained their irritability, but that when the galvanic or other stimuli were applied to the nerve higher up, they failed to elicit any response from the unpoisoned tributary muscles,—positive proof that the nerve-trunks are paralyzed by a direct action of the drug. This is seemingly opposed to the experiments of Stannius (*loc. cit.*), who concluded that prussic acid applied locally to the nerves has no effect upon them. Stannius, however, compared the results of soaking a nerve in water and in a weak solution (three to four per cent.) of prussic acid, and water thus employed is toxic to the nerve-trunks. Kölliker used, in repeating the experiments of Stannius, neutral solutions of phosphate of sodium, one containing, the other free from, hydrocyanic acid, and found that the nerves in the poisoned liquid died much sooner than did those in the non-poisoned solution.

The experiments of Kölliker are in agreement with those of Stannius, that the muscle dies very much more quickly in the solution of the acid than does the nerve, losing its excitability in from seven to eight minutes. This rapid destruction of muscular irritability by the local application of prussic acid was, I believe, first noted by Coullon in 1819. Yet it is most probable that when given internally prussic acid acts almost as rapidly upon the nerve-trunks as upon the muscles, since Kölliker noted that in some cases galvanization of the nerve was incapable of causing contractions in the tributary muscles, although the latter responded feebly to direct stimulation. This fact has been experimentally corroborated by Funke (*Berichte über die Verhandl. d. k. sachs. Gesellschaft d. Wissensch. zu Leipzig*, Bd. xi., 1859, p. 28).

Upon the peripheral sensitive nerves prussic acid probably, if in sufficient concentration, acts as a paralyzant; at least Kölliker (*loc. cit.*, p. 282) found that if the leg of a strychnized frog, whose heart had been cut out to prevent absorption, was put in a four per cent. solution of prussic acid, in a very short time irritation of the immersed skin ceased to produce convulsions.

From the slowness with which, in Kölliker's experiments, the nerve-trunks were affected in frogs poisoned by hydrocyanic acid, it seems probable that he is correct in his conclusion that in these batrachians the poison first paralyzes the brain, and then the reflex centres of the spinal cord, and afterwards the motor nerves. But I have not met with any experimental evidence in regard to the order in which prussic acid affects the nervous system. According to Kiedrowski,* as quoted by Preyer, in frogs it first paralyzes the gray, then the white substance of the brain, and the early disappearance of reflex movements is not due to spinal palsy, but to destruction of the functional power of the peripheral afferent nerves. Preyer also states that the conclusions of Kiedrowski rested upon the following experimentally proven fact, which, if accurate, seemingly renders them logically inevitable. When a frog is poisoned with prussic acid, and afterwards with strychnia in properly-proportioned doses, there is a stage at which slight irritation of the afferent nerve-roots causes violent general tetanic spasms, although the most intense peripheral irritation fails to elicit response.

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* I have, unfortunately, been unable to obtain access to the original paper of E. de Kiedrowski. Even Preyer appears to know it only in abstract. According to him, it was published in 1858, at Breslau, as a dissertation, under the following title: *De quibusdam experimentis quibus quantam vim habeat acidum hydrocyanicum in nervorum systema cerebro-spinale atque in musculos systematis vertebralis probatur.*

It is a question of interest to decide as to the cause of the convulsions in poisoning by hydrocyanic acid. I have found that they do not occur after section of the cord in parts below the point of section, and that they are therefore cerebral in origin: for reasons detailed elsewhere (see p. 143), it is very probable that they are due to disturbed cerebral circulation, and this probability is confirmed by an experiment of Laschkewitsch (*Reichert's Archiv für Anatomie*, 1868), who opened the thorax of a rabbit so as to expose the heart, maintained artificial respiration, and administered prussic acid; directly after arrest of the heart had commenced, the convulsion came on. The earlier observation of Coze (*Comptes-Rendus*, t. xxviii., 1849, p. 780) is also to the same effect, as he states that the convulsions did not occur until directly after the arrest of the circulation. In frogs poisoned with hydrocyanic acid, convulsions do not take place. Preyer states that after section of the vagi convulsions do not generally happen in mammals, but if artificial respiration be performed they come on (*loc. cit.*, p. 69).

THERAPEUTICS.—Our knowledge of the physiological action of prussic acid does not lead to a belief in its wide applicability to the relief of disease, and I think clinical experience has demonstrated that it is of little value except in meeting three indications: first, *to allay cough;* second, *to relieve irritation of the gastric nerves;* third, *to allay irritation of the peripheral sensitive nerves.*

There appears to be in the profession a very wide-spread belief in the power of this remedy to allay cough; at least it is very largely used for this purpose in cough-mixtures, either itself or in the form of cyanide of potassium. I have employed it in a great number of cases in hospital practice, and apparently with good effect, although, as it was always given in combination with such remedies as morphia, it is difficult to say how much of the result was due to it. I do not believe it can compare with such narcotics as opium or hyoscyamus in its ability to fulfil the present indication.

There can be, on the other hand, no doubt as to the value of prussic acid in certain stomachic affections, especially nervous *vomiting* and *gastralgia.* When the pain is accompanied by decided dyspeptic symptoms, the remedy will sometimes succeed, but more often fails. Even in the most favorable cases it does not always afford relief; and as the relief when it does occur is immediate, or at least is very soon apparent, it is useless to persist long in the exhibition of the remedy. In these cases its action is probably local, as it certainly is when the acid is employed to relieve itching in *prurigo* and other cutaneous diseases. For this purpose it is used as a wash (fʒss to fʒi in f℥i); but great care must be taken to avoid constitutional effects, especially when there is any abrasion of the skin. Very serious results are said to have been caused by its absorption when carelessly used in skin-diseases.

Prussic acid has been commended as an arterial sedative; but it is evident that we possess numerous more efficient and far safer remedies of such character.

TOXICOLOGY.—The symptoms of prussic acid poisoning have already been mentioned: those of most value from a diagnostic point of view are the sudden occurrence of unconsciousness; the violent convulsions; the general paralysis; the peculiar character of the breathing, expiration being prolonged and forced; and the rapid results. The odor of prussic acid upon the breath is very often, but by no means always, present. When distinct, it is, of course, of very great diagnostic value. Leaving out of sight the cyanides, the only poison with which prussic acid could well be clinically confounded is nitro-benzole. The distinction is often very difficult, large doses of the latter substance killing almost as quickly as prussic acid, and inducing analogous symptoms. Caspar advises that after death the body be left open, exposed to the air, as the odor of prussic acid disappears rapidly, whilst that of the nitro-benzole is persistent. The diseases with which the poisoning may be confounded most readily are some forms of *apoplexie foudroyante*, and sudden failure of the heart's action. The diagnosis may, during life, be almost impossible. It has been asserted that stertorous breathing does not occur in prussic acid poisoning; but it has been present in several reported cases. (See *Taylor's Principles and Practice of Medical Jurisprudence*, Philadelphia, 1873, p. 363.) An autopsy, however, ought generally to enable the physician to determine whether the case has or has not been one of prussic acid poisoning, if the symptoms during life are known.

A curious case of temporary *hemiopia*, apparently caused by the fumes of hydrocyanic acid, is reported in *Brit. Med. Journ.*, i. 1884, 409.

The period at which death may occur after the ingestion of the poison is set down by Lonsdale at from one to fifty-five minutes; but a case is reported in *Guy's Hospital Reports*, 1868, p. 259, observed by Dr. Hilton Fagge, in which the fatal result was put off for at least an hour and a quarter after the ingestion of hydrocyanic acid. After death the body often presents a livid surface, bloated countenance, fixed glassy eyes with dilated pupils, and clenched fingers; sometimes it offers nothing worthy of note except excessive rigidity, and the face may be very pale. When opened, the odor of prussic acid is generally, but not always, emitted; the mucous membrane of the stomach is very commonly found much congested, and the dark or cherry-colored liquid blood usually everywhere fills up the veins. The heart is soft and flaccid.

The treatment of poisoning by prussic acid is, unfortunately, as inefficient as it is simple. There is no known chemical or physiological antidote to it, the asserted antagonism of atropia having been disproven by the experiments of Keen (*Proc. Phil. Acad. Nat. Sci.*, 1869) and of Boehm and Knie.

The stomach should, if possible, be emptied, and the hypodermic use of atropia as a respiratory stimulant might be tried; the inhalation of the vapors of ammonia, and the free exhibition of ammonia by the mouth and by injection into the veins, may be practiced. Artificial respiration has been found very successful by Preyer, and by Boehm and Knie, in animals when poisoned by small doses of prussic acid, and should always be assiduously practiced. Next to it in importance is the use of the alternate cold and hot douche, about a half of a small bucketful of cold water and the same quantity of very hot (115° F.) water being dashed upon the chest in rapid succession.

ADMINISTRATION.—The dose of the officinal dilute prussic acid is one to three drops.

The *Cyanide of Potassium* (POTASSII CYANIDUM, U. S.) is prepared, according to the U. S. Pharmacopœia, by heating together the ferrocyanide of potassium and the carbonate of potassium. It occurs in white, amorphous, opaque masses, having the odor of prussic acid and a taste of similar character, but somewhat alkaline. It is deliquescent, and readily soluble in water. When the nitrate of silver is added to its solution, there falls a precipitate of the cyanide of silver, which is wholly soluble in ammonia.

When the cyanide of potassium is taken into the stomach, the acids there present convert it into prussic acid, and the same change probably occurs, although more slowly, even when the salt is injected directly into the blood-vessels. The physiological, therapeutical, and toxicological properties of this salt are similar to those of prussic acid.* Death, however, does not occur so soon as when hydrocyanic acid has been taken, and insensibility is sometimes not manifested for several minutes. Five grains of the salt have caused death in several cases. The therapeutic dose is one-tenth to one-twelfth of a grain.

The *Cyanide of Silver* (ARGENTI CYANIDUM, U. S.) is a white insoluble powder, which is used solely for making prussic acid.

Cyanogen Gas has been studied physiologically by Dr. B. Bunge (*Archv. Exp. Path. u. Pharm.*, xii. 71). He finds that it kills by paralyzing the centres of respiration, but is less powerful and strong in its influence than is hydrocyanic acid, and causes only very feeble convulsions.

VEGETABLE ACIDS.

Although most of the officinal vegetable acids differ so much from the other substances considered in the present class as not to be poisonous except in enormous doses, and although they are never used to produce a profound impression upon the circulation, yet since they have, or at least are believed to have, the power of lowering the force of the cardiac movements to some extent, and since they are so commonly believed to have a tendency to depress animal temperature as to be usually spoken of as *refrigerants*, the present seems to me a fitting position for their consideration. In experiments made by W. H. Gaskell (*Journ. Physiology*, iii. 49), similar to those described in the article on digitalis (see p. 150), it was found that whilst alkalies contracted the arterioles of the frog, acids* caused a dilatation, probably by paralyzing the muscular coats. Acids also diminished the activity and power of the frog's heart.

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* Poisoning is stated to have occurred from the inhalation of the vapors of the cyanide, and, in photographers, from the absorption through the hands (*Brit. and For. Med.-Chir. Rev.*, July, 1876, p. 231).

ACIDUM TARTARICUM—TARTARIC ACID. U.S.

Tartaric acid occurs in large, hard, transparent, six-sided prisms, which are pyro-electric and phosphorescent when rubbed in the dark, and are nearly free from odor, but have a very sour taste. In the shops the acid is almost always kept in the form of powder. Tartaric acid is the acid of the grape, and occurs in grape-juice as a supertartrate of potassium. When the juice undergoes fermentation and alcohol is developed, the acid salt, not being soluble in the newly-formed menstruum, precipitates, collecting as a dark mass in the wine-casks, whence it is sent into commerce under the name of *argol* or *tartar*. Out of this substance the acid is manufactured by treating with lime, so as to form a tartrate of calcium, and precipitating this new compound in its watery solution by sulphuric acid, sulphate of calcium falling, tartaric acid remaining in solution. Tartaric acid is soluble in little more than half its weight of hot water and less than its weight of cold water. It is distinguished from all other acids by forming a crystalline precipitate (bitartrate) when added to a neutral solution of potassa.

Physiological Action.—When applied to a denuded surface, or in sufficient concentration to a mucous membrane, tartaric acid acts as a very decided irritant, and even upon the skin its saturated solution after a time causes redness and burning.

When the drug is taken internally in sufficiently large doses, it acts as an irritant poison, causing violent œsophageal and gastric burning, vomiting, and, it may be, fatal gastro-enteritis. Upon animals it acts in large doses precisely as it does upon man. Thus, Mitscherlich states that three or four drachms suffice to kill a rabbit, the evident symptoms being great weakness of the heart's action, difficult and slow breathing, steadily-increasing pains, with slight convulsions before death. According to Devergie, it requires nearly half an ounce to kill a dog when given by the stomach; but Pommer (quoted by Husemann) asserts that one gramme (15.34 grains) injected into the crural vein of a dog will produce death.

Tartaric acid is never used internally by practitioners in such doses as to cause any of the symptoms above detailed, and it is evident that these symptoms throw little light upon its action in therapeutic doses, except to render it somewhat probable that the tendencies of the medicine are to lower cardiac action. This probability is increased very much by the experiments of Bobrick (quoted by Husemann, *Die Pflanzenstoffe*, p. 561), who found that very large doses render the heart's action weaker and slower.

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* Lactic acid appears to have been the only one used, and it does not appear certain that the results of experiments would be the same with all acids, as is stated in Gaskell's generalisation.

A great deal of interest to the therapeutist centres in the question as to what becomes of the acid in the system. Unfortunately, our knowledge in regard to this matter is far from complete; but the drug is probably partially burnt up in the body and partially eliminated by the kidneys. Wöhler,* in his experiments, found it in the urine in the form of tartrate of calcium, whilst Buchheim* and Piotrowski* could find only a very small percentage of the ingested acid in the urine, and conclude that it is mostly destroyed in the body. Dr. Münch (*Archiv des Vereins für Gemein. Arbeiten*, 1863, p. 370) finds that when tartaric acid or citric acid is given it soon appears in the urine. Dr. H. Bence Jones (*Medical Times and Gazette*, vol. ix., 1854, p. 408, and *Lectures on Pathology and Therapeutics*, London, 1867) has found that both citric acid and tartaric acid cause a very great increase in the acidity of the urine of persons taking them, and are apt also to give rise to the presence of free uric acid in the excretion. Unfortunately, Dr. Jones did not attempt to determine whether the increased acidity was or was not due to the presence of the vegetable acid in the urine.

THERAPEUTICS.—Tartaric acid is very rarely used in medicine, the citric acid almost always being preferred. It may, however, be employed whenever it is desired to render the urine acid, in doses of ten to twenty grains; but it is less valuable than the acid of the lemon.

TOXICOLOGY.—There are, I believe, but three fatal cases of tartaric acid poisoning on record: one reported by Devergie (*Ann. d'Hygiène*, 1851, t. ii.); one by Prof. Taylor (*Principles and Practice of Medical Jurisprudence*, London, 1873, p. 230), in which death took place nine days after the ingestion of an ounce of the poison dissolved in half a pint of water; and one (*Med. Press and Circular*, Nov. 1880) in which a half-ounce of the acid was *supposed* to have been taken. The treatment of tartaric acid poisoning consists in the free exhibition of magnesia, of lime, of the carbonate of potassium or of sodium, or of any article, such as soap, containing an alkali in a suitable shape, which may be at hand. The after-treatment is that of toxic gastro-enteritis.

ACIDUM CITRICUM—CITRIC ACID. U.S.

Citric acid is the acid of lemon- and lime-juice, from which it is extracted by a process precisely similar to that employed in the manufacture of tartaric acid. It occurs in rhomboidal prisms, which are sometimes very large, are nearly free from odor, but are possessed of a very sour, almost corrosive taste, which, when the acid is in sufficiently weak solution, is quite pleasant.

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* All these are quoted by Husemann, *Die Pflanzenstoffe*. I have not seen the originals.

Citric acid is soluble in three-fourths of its weight of cold water, half of its weight of boiling water, soluble in alcohol, insoluble in ether.

It is sometimes adulterated with tartaric acid, which may be readily detected by the addition of a strong neutral solution of carbonate of potassium to a strong solution of the suspected drug, when, if tartaric acid be present in any amount, a precipitate of the bitartrate is formed.

PHYSIOLOGICAL ACTION.—Citric acid in concentrated solution certainly acts upon abraded surfaces and upon mucous membranes as an irritant, but, according to Mitscherlich, is less irritant than tartaric acid, since its concentrated solution has no action upon the sound skin.

No case of poisoning by citric acid has occurred in man, that I am aware of, and Piotrowski (quoted by Husemann, *Die Pflanzenstoffe*, p. 561) took, in six hours, thirty grammes, an hour later fifteen grammes, and an hour later thirty grammes, or nearly two ounces and a half in all, with the induction of no more serious symptom than vomiting. It is, therefore, somewhat doubtful whether citric acid is capable of causing death in man. This difference in action between it and tartaric acid may depend upon the latter being so much the more irritant of the two; upon the urinary secretion their action is probably similar.

Hugo Schulz states that citric acid is an active antiseptic, a five per cent. solution being sufficient to preserve small pieces of meat for two weeks; one part in a thousand was fatal to paramecia (*Deutsch. Med. Wochens.*, 1883, ix. 398).

THERAPEUTICS.—Citric acid is sometimes itself employed in medicine, but is almost exclusively used in the form of *Lemon-juice* (SUCCUS LIMONIS), which some, it is true, have thought to be dependent upon citrate of potassium for much of its virtue, but which contains, as shown by the analysis of Prof. H. Bence Jones (*Medical Times and Gazette*, vol. ix., 1854), in every ounce twenty-six or twenty-seven grains of free citric acid, and not two grains of the citrate of potassium.

Lemon-juice has several very distinct uses in medicine, all of them resting upon clinical rather than physiological data. The chief and most important of these is in the cure and prevention of *scurvy*. During the disease it should be drunk freely in the form of lemonade, three or four ounces of it being taken daily. As a prophylactic against the disease, lemon-juice is simply invaluable; but it is absolutely necessary that it be of good quality. It may be prepared for long voyages in one of two ways: first, boil the juice slightly, strain, allow to cool, pour into bottles up to their necks, fill the vacant space above with pure olive oil, cork tightly, and keep the bottle upright; second, add ten per cent. of brandy, and bottle as before (*Medical Times and Gazette*, 1854, p. 635). Citric acid is of some value in scurvy, but is incomparably less active than lemon-juice. In *acute rheumatism*, benefit may be derived from the free use of lemon-juice, as originally proposed by Dr. Rees, of London. One or two ounces of it may be given four or five times a day; but it is certainly less efficacious than the alkalies. In *catarrhal jaundice*, and in habitual *torpor of the liver*, the free internal use of lemon-juice often aids in effecting a cure. In *fevers*, lemonade often affords a very refreshing and useful refrigerant drink.

ADMINISTRATION.—Lemon-juice, when it can be had, should always be preferred to citric acid; when only the latter is available, an artificial lemon-juice may be made by dissolving in a pint of water an ounce of the acid with which four drops of the oil of lemon have been well rubbed up.

ACETUM—VINEGAR.

The physical properties of vinegar are too well known to need description here. That best suited for medicinal use is in this country prepared from cider, and should have a trace of the taste of cider. It is sometimes adulterated with sulphuric acid, which may be at once detected by boiling with chloride of calcium, which precipitates any free sulphuric acid as sulphate of calcium, without affecting the small proportion of soluble sulphates existing in vinegar. Vinegar may be substituted for lemon-juice as the basis of an acidulous drink in fever when the lemon-juice is not to be had; but as an *antiscorbutic* it is certainly very much inferior to it, and has not, that I am aware of, been tried in *rheumatism*.

Acetic Acid (ACIDUM ACETICUM, U.S.) is a colorless liquid, having a pungent odor, free from empyreuma, and an intensely acid, corrosive taste. It contains thirty-six per cent. of the monohydrated acetic acid, and has a specific gravity of 1.047. Glacial or monohydrated acetic acid is not officinal. It is a colorless liquid, crystallizing at 34° F., and actively escharotic,—in a measure, no doubt, owing to its properties of dissolving gelatine and gelatinous tissue and of effecting a partial solution of albuminous matters. *Dilute Acetic Acid* (ACIDUM ACETICUM DILUTUM) is officinally prepared by the addition of seven parts of water to one part of acetic acid, and should have the sp. gr. 1.006. *Acidum Aceticum Glaciale*, U. S., *glacial* or *absolute acetic acid*, is at 59° F. a crystalline solid.

Dilute acetic acid, or its equivalent, vinegar, is a useful topical application in various superficial inflammations of the skin, such as "*sunburn*," and in *sprains*. Applied to the skin, it acts as a powerful stimulant and astringent, causing contraction of the vessels and great whiteness. Diluted with two or three times its bulk of water, it is occasionally employed as an injection against *seat-worms*; but the infusion of quassia is preferable.

The use of acetic acid as a caustic will be spoken of under the heading of Escharotics.

TOXICOLOGY.—Acetic acid in any of its more concentrated forms is a corrosive poison, and death has been produced by it in at least one case (Orfila, *Toxicologie*, t. ii.). The symptoms resemble those caused by mineral acids, and the treatment is exactly similar,—neutralization by an alkali or its carbonate, or by some substance, such as soap, containing an alkali, and the meeting of indications as they arise.

Oxalic Acid (ACIDUM OXALICUM), although never used in medicine, has so frequently caused death by its poisonous influence as to merit notice here. In 1874 (*Gaz. Méd.*, p. 92) Rabuteau announced that in oxalic acid poisoning the nerves and muscles are not affected, and that therefore the acid acts upon the nerve-centres. This has been confirmed by the elaborate researches of Drs. R. Kobert and B. Küssner (*Virchow's Archiv*, Bd. lxxviii. 109), who find that it paralyzes the respiratory, vaso motor, and other motor spinal centres. The acid is eliminated by the kidneys. As a poison, oxalic acid figures in two forms: that of simple oxalic acid, and that of the *acid oxalate of potassium*, or *salt of sorrel*, or *essential salt of lemons*, as it is variously termed in common parlance. The symptoms produced are a hot acrid taste experienced during the swallowing, a burning in the gullet, soon extending to the stomach, intense abdominal pain, vomiting of highly acid, greenish, blackish-brown or bloody mucus (rarely of arterial blood), collapse, livid surface, cold skin, entire prostration of strength, small irregular pulse, stupor, unconsciousness, sometimes convulsions (cases, *Guy's Hosp. Reports*, 1838, iii.; *Dublin Hosp. Reports*, 1818, ii.), and finally death. In some cases the gastric symptoms are very prominent; in others they are nearly wanting, and the chief manifestations are collapse and such nervous symptoms as almost complete general paralysis, numbness, and finally stupor; indeed, the patient may suddenly fall unconscious immediately after the ingestion of the poison (case, *Guy's Hosp. Reports*, 1874). According to Taylor, the smallest quantity which is known to have caused death is one drachm. An ounce usually proves fatal, but has been recovered from. After death the coats of the stomach are usually found softened and swollen, and sometimes perforated (case, *Edinb. Med. Journ.*, vii., July, 1861). Dr. Rabuteau (*Gaz. Méd.*, 1874, p. 93) affirms that the blood is everywhere scarlet; but this is certainly not always the case (case, Taylor, *Med. Jurisprudence*, i. 224). According to Kobert and Küssner, the urine during life contains some strongly reducing substance of unknown nature, oxalate crystals in abundance, and usually albumen and tube-casts. A pathognomonic post-mortem lesion is, according to the same investigators, the incrustation of the urinary tubules with crystals of oxalates. In poisoning by oxalic acid, the immediate administration of an antidote is of the utmost importance. As the oxalates of potassium and of sodium are poisonous, neither potash nor soda is available; but fortunately lime or chalk is a perfect antidote to oxalic acid, forming the excessively insoluble oxalate of calcium. As time is a matter of so much importance, very often it is best simply to scrape the whitewash off a wall, ceiling, fence, or wherever it may be at hand, rub it up hastily with water, and administer it freely. The after-treatment is that of toxic gastro-enteritis.

CLASS V.—ANTISPASMODICS.

Under the name of *Antispasmodics* are grouped in this treatise a number of medicines generally of very feeble powers, but of frequent use. In certain conditions of the nervous system—conditions associated with weakness rather than with simple depression—the nerve-centres appear to be more susceptible than is normal to external impressions, as well as to those impulses which originate in the cerebral centres themselves and are connected with the emotions. As a result of this state, various symptoms arise, of trifling import, but often apparently severe, and always annoying. Such symptoms, in their mildest form, constitute the state of unrest known as *nervousness;* in their severer type they may rise in intensity up to the wildest convulsion of *hysteria.* It is in this class of affections that the so-called antispasmodics are useful. As the condition which they relieve is always associated with weakness, they are often spoken of as "nervous stimulants." In regard to most of them there is but little evidence of their increasing power or functional activity when given to healthy individuals. Some of them act very slightly upon the circulation when given in very large doses, and a few when administered as freely as possible induce slight cerebral symptoms, such as vertigo; but, excepting camphor, caffein, and Hoffman's Anodyne, none are capable of producing serious poisoning. As any theory of the method in which the hysterical convulsion originates—of its immediate causes and the mechanism of its production—would, with our present knowledge, be at best but an ingenious speculation, the safest plan in regard to the action of drugs belonging to the class now under consideration is to accept the teachings of clinical experience as to facts, and to avoid theorizing as to the way in which the results are brought about.

MOSCHUS—MUSK. U.S.

A highly odorous, unctuous substance, obtained from the glands situated just in front of the preputial orifice of the Moschus moschiferus, or musk-deer of Thibet. The genuine musk-sac is to be distinguished from imitations of it by the hairs being arranged concentrically around a minute orifice. As it occurs in commerce, musk is very greatly adulterated.

Physiological Action.—Musk appears to act upon the nervous system simply as a mild stimulant and antispasmodic. Jörg and Sundelin have experimented with it upon healthy men with somewhat contradictory results

According to the first-named observer, twenty grains of it induce exhilaration without lassitude, but, according to the latter authority, may cause giddiness, drowsiness, and lassitude. Both observers noted a slight increase in the frequency of the pulse. It seems to me evident that the action of musk upon the organism is a very feeble and uncertain one. Yet there is considerable clinical evidence that when the nervous system is exhausted it is of service in calming restlessness and equalizing the disturbed balance of nervous power.

THERAPEUTICS.—Musk is at present very little used, but it is strongly recommended by some of the older writers in various spasmodic affections, especially in *hysterical convulsions.* In *hiccough* it has been considered a specific. In the *delirium of low fevers* it is sometimes valuable; and it has been especially commended by Trousseau in the *ataxic pneumonia* of drunkards, when the nervous symptoms are out of proportion to the local disease. The dose of musk is from five to fifteen grains, which may be given suspended in mucilage. *Tincture of Musk* (*Tinctura Moschi,*—1 to 10, U. S.) is given in doses of one-half to two fluidrachms.

CASTOREUM—*Castor.*—The preputial follicles of the beaver are pyriform sacs, occurring in pairs, and containing an unctuous material,—the *castor.* This is a substance allied to musk in its physical properties, and apparently also in its medicinal qualities. It is certainly less efficient, however, than musk, and Mr. Alexander (*Pereira's Materia Medica,* American edition, 1866, p. 949) is said to have taken a quarter of an ounce of it without having experienced any effect. It is employed in the same affections as musk, in doses of fifteen to sixty grains, suspended in mucilage. There is an officinal *tincture,* which is stronger in alcohol than in castor.

VALERIANA—VALERIAN. U.S.

The root of the Valeriana officinalis, an herbaceous perennial of Great Britain. It consists of a short, yellowish-white rhizome, with numerous fibrous roots, of a bitter taste and peculiar odor. The active principle of valerian appears to be the *oil of valerian,* which, according to Pierlot, consists of a mixture of valerian camphene, valerian camphor, valerianic acid, resin, and water.

PHYSIOLOGICAL PROPERTIES.—Upon cats valerian has a very extraordinary effect, attracting them strongly, and greatly exciting their sexual passions. It is possible that this action is suggestive, due rather to the resemblance of the odor to that of the animals during sexual excitement, than to a direct action of the drug. Valerianic acid given to rabbits in large doses produces, at first, a slight acceleration of the pulse, which, with the respiration, afterwards becomes less frequent than normal, and at the same time lassitude and muscular weakness are developed. Enormous doses kill rabbits somewhat suddenly, or produce fatal gastro-enteritis.

Upon man, large doses (ʒii to ʒiv) are said to produce a feeling of warmth in the stomach, and sometimes nausea, vomiting, and colicky pains. The pulse is generally slightly quickened, and a sense of exhilaration is induced, accompanied, however, by formication in the hands and feet. Very large amounts cause a feeling of heaviness, and even of pain, in the head.

THERAPEUTICS.—Clinical experience has demonstrated the value of valerian as a means of relief for the milder forms of functional disturbance dependent upon a weak and over-excitable or an exhausted nervous system. In the state of unrest familiarly known as "*nervousness*," by soothing and quieting the patient, it will often indirectly procure sleep.

In *hysteria* it has been the most frequently used of medicines, and its action is ofttimes most happy.

It has also been employed, but with more doubtful advantage, in *mania a potu*, and in the *delirium of adynamic fevers*. In these cases it is almost invariably conjoined with more powerful remedies, and it is very difficult to decide how far it assists in procuring the beneficial result.

ADMINISTRATION.—The best preparations of valerian are the *fluid extract* (*Extractum Valerianæ Fluidum*, U. S.), dose, one fluidrachm; and the *ammoniated tincture* (*Tinctura Valerianæ Ammoniata*, U. S.,—℥ii to Oj), dose, one to three fluidrachms. The dose of the *infusion* is a wineglassful; that of the simple *tincture* (*Tinctura Valerianæ*, U. S.,—℥ii to Oj) is one to three fluidrachms.

ACIDUM VALERIANICUM.—*Valerianic Acid* is an oily, colorless liquid, of a caustic taste, and a strong odor, resembling, but differing from, that of valerian. It is made by the action of chromic acid upon amylic alcohol, by a somewhat complicated process, and is employed for the manufacture of *Valerianate of Ammonium* (*Ammonii Valerianas*, U. S.), a white salt occurring in quadrangular plates, which effloresce in a dry and deliquesce in a moist atmosphere, have the odor of valerianic acid and a sharp sweetish taste, and are very soluble in water and in alcohol.

THERAPEUTICS.—This salt was introduced by M. Déclat, of Paris, as a remedy for *neuralgia*. It has since been used very largely for *nervous headache* and in *hysteria*. It appears to be about equivalent to valerian, but, unless it be in nervous headaches, is less efficient. The dose of it is ten grains, which is generally administered in the form of an *elixir*.

ASAFŒTIDA—ASSAFETIDA. U.S.

An exudation obtained by incising the living root of the Narthex Assafœtida, an umbelliferous plant of Afghanistan. It mostly occurs in irregular opaque masses of a dull yellowish- or pinkish-brown, white when freshly broken, of a bitter acrid taste and a strong garlicky odor. Even this *lump assafetida* is largely composed of tears agglutinated together; sometimes these tears are distinct and separate, when they constitute the variety known as *assafetida in tears*. Assafetida is composed chiefly of gum and resin, but its properties are in great part due to the volatile oil, of which it contains from 3.5 to 4.5 per cent.

PHYSIOLOGICAL ACTION.—When taken into the stomach, assafetida acts as a local stimulant and carminative, and on this account is in some parts of the East used as a condiment. The oil is without doubt absorbed. The evidence as to its action upon healthy men is both scanty and contradictory. Thus, whilst M. Pidoux took half an ounce in a single dose without perceptible effects other than to render his secretions horribly offensive for two days, Jörg and his disciples found that in twenty-grain doses it produced gastric uneasiness and pain with alvine dejections, increased the pulse-frequency and animal warmth, quickened the respiration, and caused headache, giddiness, and erotic excitement.

THERAPEUTICS.—Clinical experience has abundantly proven that assafetida is one of the most efficient of the so-called antispasmodics, and may be given to fulfil the same indications as valerian in *functional spasm*, in *hysteria*, and in *nervousness*. It differs from valerian in having a much more decided action upon the mucous membranes. It is an excellent *carminative*, and in the form of injection is constantly used for the relief of *tympanitis*. It also in small doses increases the appetite, and affords relief in the *dyspepsia*, with flatulent colic and costiveness, of the aged or hysterical. As a *stimulating expectorant and antispasmodic*, it is useful in *whooping-cough* and in *chronic catarrh*. It is especially efficient in palliating the latter affection as occurring in old people, when the difficulty of breathing is paroxysmally increased by spasm of the bronchial tubes. In *infantile convulsions* and in *severe infantile colic*, assafetida enemata (fʒii to f℥ss of the milk) are exceedingly useful and harmless.

ADMINISTRATION.—The *Pills of Assafetida* (*Pilulæ Assafœtidæ*, U.S.) each contain three grains: from two to four may be given at once.

The dose of the *mixture* or *milk of assafetida* (*Mistura Assafœtidæ*, U.S., —ʒii to Oj) is half to one fluidounce; for injections, one to three fluidounces; that of the *tincture* (*Tinctura Assafœtidæ*, U.S.,—℥ii to Oj), half to one fluidrachm. The *suppositories* contain the equivalent of forty minims of the tincture. *Emplastrum Asafœtidæ*, U. S., is used externally.

CAMPHORA—CAMPHOR. U.S.

Camphor is obtained in China, Japan, Cochin China, the Sunda Islands, etc., by boiling the comminuted wood of the root, stem, and branches of the Laurus Camphora, and skimming off the camphor as it rises to the surface of the water when cold. This camphor is then partially purified by sublimation, and comes into commerce as *crude camphor*, which is in grains of a whitish or pinkish color, and is finally purified by sublimation with lime.*

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* A variety of camphor, as well as of camphor oil, yielded by the Dryobalanops Camphora, is very highly valued in the East, but does not reach this country. For a physiological study of it, by Paolo Pellacani, see *Arch. Exper. Pathol. und Pharm.*, xvii. 376.

Refined camphor (or, as it is commonly called, *camphor*) occurs in disks or hemispherical bowl-like translucent masses, of a fibrous or granular fracture, Its taste is hot and peculiar; its odor very strong and characteristic; it is volatile, inflammable, tough, but readily pulverized on the addition of a few drops of alcohol; melts at 347° F.; is soluble in one thousand parts of cold water,[*] in one part of strong alcohol, and still more soluble in chloroform; thrown upon water, a granule of camphor floats, and exhibits a rotary motion.

By slow sublimation at ordinary temperatures, camphor can be made to crystallize in handsome hexagonal tables.

PHYSIOLOGICAL ACTION.—Locally applied, camphor is a decided irritant, although when it is taken into the mouth a sense of coolness after a time is experienced, due no doubt to the volatility of the drug: a precisely analogous phenomenon occurs with some other volatile irritants, such as oil of peppermint.[†]

Great differences of opinion have prevailed in regard to the action of camphor upon man, and it is scarcely doubtful that it acts differently upon different persons, or at least that doses which in some cause only exhilaration in others produce general depression. When a moderate dose (five to ten grains) of camphor is taken, a feeling of exhilaration is usually induced, a sense of comfort and quietness, especially marked in those previously suffering from "nervousness;" the pulse may be somewhat accelerated, although it is undoubtedly not markedly affected in the majority of cases, and Trousseau saw it fall after the ingestion of ten grains of the drug. After larger doses (twenty to thirty grains) the pulse is usually lowered in frequency, and giddiness, with a feeling of lassitude, is produced, preceded, it may be, by a short period of exhilarative excitement. After poisonous doses (thirty to sixty grains) the symptoms, which are tolerably uniform, are as follows: faintness, headache, vertigo, confusion of ideas, burning pain in the stomach, delirium, violent convulsions, insensibility, apparent general paralysis; a pulse generally small, but sometimes accelerated and sometimes lowered in number; a skin cool, pale or livid, generally bedewed with sweat. Sudden unconsciousness, with or without convulsions, has been in some instances the first manifestation of the action of the poison, and, of course, in any individual case many of the symptoms narrated above may be wanting.[‡]

No death has occurred in the adult directly from camphor. A young, sickly infant was killed by ten grains of it; and a woman four months gone in pregnancy, having taken three drachms of camphor, suffered the usual symptoms, followed by an abortion which proved fatal.

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[*] By rubbing the gum up with magnesia in water, the latter can be made to take up much more than one part in one thousand.

[†] For physiological action of *Camphor-Cymol*, see *Arch. Experim. Path. und Therap.*, 1873, Bd. i.

[‡] Cases, *Edinburgh Med. Journal*, May, 1873; *The Clinic*, March, 1873; *Weiner Medizinische Presse*, 1874, p. 258; *Berlin. Klin. Wochens.*, Sept. 1873–74; *Trans. Lond. Clin. Soc.*, 1874, p. 27; *London Lancet*, 1876, ii. 71; *Brit. Med. Journ.*, Feb. 1875; also 1877, i. 607.

Much contradictory evidence might be adduced as to the influence of camphor upon the genital organs. The truth evidently is that its action varies according to the dose and the idiosyncrasies of the patient. In the great majority of instances, I think, camphor in moderate doses has no decided influence upon the sexual system; at least I have seen many hundred such doses taken and have never yet seen any aphrodisiac effect. In some persons, however, full therapeutic doses are said to cause sexual excitement. In regard to very large doses, the testimony is quite uniform that if they exert any action it is to lessen the erotic feelings.

Camphor acts upon articulates as a violent poison; in birds, according to Menghini, it causes stupor or delirium with epileptiform seizures; in mammals it produces symptoms similar to those seen in man, such as vomiting, violent convulsions, coma, and death, apparently from asphyxia. The convulsions must be of cerebral origin, as, according to the experiments of C. Weidemann (*Arch. Exp. Pathol. und Therap.*, vi., p. 216), and of Hoffmann (quoted by Weidemann), they do not occur after section of the cord in portions of the body below the point of division. Whether they are the result of a direct action upon the cerebrum is not determined, but the other symptoms produced by camphor indicate that the drug has a decided influence upon that organ. In frogs, Weidemann found that the convulsions are masked by a general paralysis, chiefly due to a depressant action upon the motor nerves; the spinal cord, however, also suffering in its functional activity, the muscles escaping. The action of toxic doses of camphor upon the circulation is decided. In the poisoned frog the cardiac beats become slow and powerful, and as Heubner found (*Arch. Exper. Path. und Therap.*, v., p. 427) the camphor was able to excite the heart when arrested by muscarin, it is probable that its action is upon the heart itself. The same investigator failed to get any rise of arterial pressure in rabbits; but in the more extended researches of Weidemann it was found that in the convulsive stage of camphor-poisoning there is a very marked rise of the arterial pressure, which is largely due to the convulsions and disturbance of breathing, as it is in a measure prevented by curarization and artificial respiration. Under these circumstances, however, sudden periodical elevations of all of the arterial pressure occur. The cause of this phenomenon is not obvious, as Weidemann affirms that it is prevented by section either of the cord or of the vagi. As, after section of the cord, toxic doses of camphor lessen the arterial pressure, it would seem probable that it is directly depressant to the heart.

Camphor is undoubtedly very much changed in the organism; the most important of its derivations is *campho-glycuric acid*, discovered by Schmiedeberg and Meyer (*Zeitschrift. f. Physiol. Chem.*, 1881), which, by warming with muriatic or sulphuric acid, is changed into *Campherol*,* a crystallizable substance soluble in ether and also in water.

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* For a physiological study of campherol, see *Archiv f. Exper. Path.*, xvii. 372.

THERAPEUTICS.—Camphor is very largely used internally as an antispasmodic, to quiet restlessness and "*nervousness.*" It is also employed in certain painful affections seen in those persons who are especially liable to the condition of the nervous system just mentioned: thus, it is often useful in *nervous headaches* and *dysmenorrhœa.* Indeed, in the latter disease, either alone or combined with opium in bad cases, it is a most valuable drug, but must be given freely. In *diarrhœa* not dependent upon inflammation, in *cholerine,* and even to some extent in *cholera,* camphor is a very efficient remedy, allaying intestinal pain and spasm, and also checking intestinal secretion. It enters into a large proportion of the popular cholera-mixtures. In *adynamic fevers* it has been very greatly employed, but is of doubtful advantage: still, a good deal of testimony could be adduced in favor of its usefulness in sustaining the system in the low stages of these diseases; and in nervous restlessness occurring at such times it is often very soothing. In *abnormal sexual excitement,* and in *chordee,* large doses of camphor very often appear to act most happily. The drug has also been very frequently exhibited in various spasmodic affections, such as *whooping-cough, epilepsy,* and even *puerperal* and *strychnic convulsions,* but is, I believe, at present never so employed. In *hysterical convulsions,* as in other phenomena of the same origin, camphor is a useful antispasmodic.

Externally, camphor is much used in liniments as a stimulant application for *bruises, sprains,* etc.

ADMINISTRATION.—Large doses (ten to fifteen grains) of camphor are best administered in emulsion, because when given in this way, being very finely subdivided, they create as little irritation as possible, and are rapidly absorbed; smaller doses may be given in pill. As an antispasmodic, the *Camphor Water* (*Aqua Camphoræ,*—1 to 125, U. S.) is usually preferred; its dose is half a fluidounce to two fluidounces, but, when a decided effect is desired, the *Spirit of Camphor* (*Spiritus Camphoræ*—1 to 10, U. S.) is preferable: its dose is half a fluidrachm to a fluidrachm. For external use, the U. S. Pharmacopœia recognizes the *Linimentum Camphoræ* (camphor one part, olive oil six parts) and the *Linimentum Saponis,* or *Soap Liniment,*—a mild liniment, very popular by itself, or as the basis of more stimulating preparations.

OLEUM CAMPHORÆ.—*Oil of Camphor* is the volatile oil of the Camphora officinarum. As it occurs in our market, it is a reddish or yellowish-brown liquid, having a strong odor of camphor, and a hot, camphoraceous taste. It contains camphor in solution, and is probably equivalent to it in physiological action, except that it is locally more stimulating, and therefore preferable in intestinal disorders. The dose is five to ten drops.

CAMPHORA MONOBROMATA. U. S.—*Monobromated Camphor,* or *Bromated Camphor.*—With iodine and bromine camphor unites to form compounds. According to Laurent, *bromcamphor* occurs in red orthorhombic crystals. These when exposed to the air undergo rapid spontaneous decomposition, but by heating in a closed vessel are resolved into hydrobromic acid, and a compound in which one atom of hydrogen in the camphor has been replaced by bromine. This bromated camphor is a crystalline solid, or occurs in large acicular crystals several inches long.

Our present knowledge of the physiological properties of bromated camphor rests upon the work of Bourneville (*Le Progrès Méd.*, 1874; also *Compt.-Rend.*, Août, 1875), of Lawson (*Practitioner*, 1874, 1875), of Pathault (*Bromure de Camphor*, Paris, 1875), of Richard Peters (*Schmidt's Jahrb.*, Bd. ci. 126), and of Pellicani (*Ibid.*). In frogs there is progress in loss of reflex excitability and of voluntary movement (Peters), which, according to Pellicani, is due to paralysis of the motor nerves. Death is caused by arrest of respiration (Peters). In mammals it produces violent convulsions, muscular weakness passing almost into paralysis, reduction of temperature (after small doses preceded by a rise—Peters), great decrease in the rate of the respiration and of the pulse, with occasional periods of hurried respiration (Peters), profound sleep or stupor, and finally death. Bourneville states that the blood-vessels of the eyes and ears are diminished in calibre. Upon man the drug probably acts as upon other warm-blooded animals; in a case reported by M. Rosenthal (*Schmidt's Jahrb.*, Bd. ci. 127), forty-five grains of it caused tremblings, marked slowing of the pulse, and coma of six hours' duration.

THERAPEUTICS.—Bromated camphor was first introduced by Prof. Deneffe (*Presse Médicale Belge*, 1871) as a nervous sedative, and as a useful antispasmodic, especially in *delirium tremens*. It has not, however, sustained its first rapidly acquired reputation, and is but little used. I have seen it do good in *spermatorrhœa*, and it may be tried in *chordee*, but especially in *hysteria* and allied convulsive disorders. It is taken with difficulty, and is apt to irritate the stomach. Bourneville proposes the following formula for hypodermic use, but Lawson states that it is so pungent that it cannot be employed: Bromated camphor, gr. xlv; Alcohol, fʒix; Glycerin, fʒvss. The dose of the drug is five to ten grains, given after meals in capsule or coated pill, and repeated as necessary. In Bourneville's experiments twelve grains injected under the skin of a cat caused death in seventy-two hours.

Carbolated Camphor.—When fifteen grains of carbolic acid dissolved in an equal quantity of alcohol are rubbed up with thirty-five and a half grains of camphor, an oily, pale-yellow liquid with a feeble odor of camphor results. This does not mix with water or glycerin, but does with almond and olive oil. It has been proposed by Dr. Soulez as a non-irritant, antiseptic dressing for wounds (see *Amer. Journ. Med. Sci.*, July, 1877, or *Lond. Med. Record*, May, 1877).

SUCCINUM—AMBER.

Amber is a fossil resin found on the southern coasts of the Baltic and in other portions of the world. It is not itself officinal or used in medicine, but by destructive distillation yields an empyreumatic oil which is included in the Materia Medica list of the U. S. Pharmacopœia.

OLEUM SUCCINI—OIL OF AMBER. U.S.

Oil of amber is an amber-colored liquid, of a hot taste, and a very strong, disagreeable odor. As kept in the shops it is said to be usually sophisticated. It is a powerful local irritant, and has been used as a rubefacient in chronic *rheumatism* and similar disorders. It is also an efficient antispasmodic, and as such is used in *hysteria*, in *whooping-cough*, and in *infantile convulsions*. In the *bronchitis* of infants, with severe nervous symptoms, as well as in the two affections last named, it is very useful as a counter-irritant and nerve-stimulant when diluted with from one to three parts of olive oil and freely applied over the spine. In obstinate *hiccough*, given by the stomach, it is probably, next to musk, the most efficient remedy. Dose, ten to twenty drops, given in emulsion.

SPIRITUS ÆTHERIS COMPOSITUS—COMPOUND SPIRIT OF ETHER. U.S.

Hoffman's Anodyne consists of alcohol a pint, ether half a pint, and ethereal oil six fluidrachms. It is a colorless, inflammable liquid, of an aromatic, ethereal odor, and a burning, slightly-sweetish taste. Its specific gravity is 0.815. Hoffman's Anodyne is sometimes offered for sale without the ethereal oil. Forty drops of the genuine preparation will render a pint of water distinctly milky; but if no oil of wine be present, milkiness will not occur. *Ethereal oil* (*Oleum Æthereum*, U. S.) is a transparent, nearly colorless, volatile liquid, of a peculiar aromatic odor, and sharp, bitter taste. Its specific gravity is 0.91. It is *heavy oil of wine*, prepared by the action of an excess of sulphuric acid on alcohol, and diluted with equal parts of strong ether.

THERAPEUTICS.—We have little or no knowledge in regard to the action of heavy oil of wine upon the system. Clinical experience has shown that Hoffman's Anodyne is more persistent in its effects upon the nervous system than an equivalent amount of ether. It is a very efficient carminative, and is also a most useful antispasmodic in all the disorders for which such remedies are employed, especially when there is a tendency to failure of the circulation, as in *valvular cardiac disease*. The dose is one or two fluidrachms, repeated in half an hour or an hour if required, and given in cold water.

HUMULUS—HOPS. U.S.

The strobiles of Humulus lupulus, or the hop-vine, cultivated in northern and middle Europe and in the United States. Hops are soft, greenish cones, one or two inches in length, composed of thin, leaf-like, imbricated scales, having a bitter taste and a heavy narcotic odor. At the bases of the scales is a yellowish powder, officinal under the name of *Lupulinum*. *Lupulin* is in minute grains, and contains, according to Payen, 2 per cent. of volatile oil, 10.30 per cent. of bitter principle, and 50 to 55 per cent. of resin. Volatile oil of hops is yellowish, and has a strong odor of the drug, and an acrid taste. The bitter principle has been obtained by Lermer in brilliant rhombic columns, of an acid reaction.

THERAPEUTICS.—Hops are a bitter tonic, and a very feeble narcotic, producing, when taken very freely, some heaviness, and perhaps sleep. They are especially useful as tonics in cases of nervous irritability requiring medicines of the class. In *delirium tremens* they are very largely used to quiet nervous irritability, to aid more powerful remedies in procuring sleep, and at the same time to strengthen digestion. In *priapism*, in *irritation of the bladder*, and in *abnormal sexual excitement*, hops have been exhibited with asserted benefit. They may be tried in large doses, but very often will fail.

Externally, hops are employed in the form of poultice, and when fresh certainly seem to aid the heat and moisture in allaying pain.

ADMINISTRATION.—The dose of the *tincture* (*Tinctura Humuli*—1 to 5, U. S.) is half a fluidounce to three fluidounces. For a decided narcotic effect the practitioner may use either the *oleoresin of Lupulin* (*Oleoresina Lupulinæ*, U. S.), dose, ten minims to a fluidrachm, in pills if desired, or the *fluid extract* (*Extractum Lupulinæ Fluidum*, U. S.), dose, half a fluidrachm to two fluidrachms.

A *hop poultice* is sometimes made by simply moistening with hot water the hops contained in a gauze bag of the required size and shape. In some cases a mixture of the broken strobiles with an equal part of Indian meal affords a more eligible preparation.

LACTUCARIUM. U. S.

The concrete juice of the Lactuca sativa,* or garden lettuce, occurs in two forms in our markets. The English variety is in small irregular pieces about the size of a pea; the German, in masses of about an inch long and half an inch in thickness. The color varies from a dark reddish-brown to a light yellowish-brown. The odor is faintly narcotic, the taste bitter. It contains a bitter, crystallizable principle, *Lactucin*, probably first discovered by Aubergier, but especially investigated by Ludwig and Kromayer (*Archiv Pharm.*, cxi.).

THERAPEUTICS.—Lactucarium is certainly a very feeble drug. Bouchardat gave half an ounce to a dog, with merely negative results; and in a number of trials made with it some years since I was unable to perceive that it exerted any influence. A very large amount of testimony exists to the same effect; but, on the other hand, various observers have claimed that it exerts a peculiar soothing, hypnotic influence, like to, but much less intense than, that of opium, and free from its disagreeable after-effects, such as depression, nausea, constipation, etc. It may be that the drug varies greatly according to age, time and mode of preparation, etc.

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* For case of reputed poisoning by Lactuca virosa, see *Schmidt's Jahrb.*, Bd. 171, p. 137

Lactucin has been experimented with by Fronmüller, who found it proportionately less hypnotic than the crude drug (*Deutsches Klinik*, 1865). The usually assigned dose of lactucarium is thirty grains, of the *fluid extract* (*Extractum Lactucarii Fluidum*, U. S.) half a fluidrachm. Much larger quantities may be given with little effect.

CIMICIFUGA—BLACK SNAKEROOT. U.S.

The root of Cimicifuga racemosa, an indigenous herbaceous plant, growing abundantly in rich, shady woods, attaining a height of six or seven feet, and readily distinguished by its very large multi-compound leaves and its long-branched spikes of whitish polyandrous flowers, naked when open. The root consists of a knotted head, with numerous fine, brittle rootlets; the odor is faint, the taste bitterish, somewhat astringent and acrid. It has not yet been determined exactly upon what the activity of cimicifuga depends. Mr. Geo. H. Davis has found in it a volatile oil, which Prof. Geo. B. Wood thinks is very probably active, since the virtues of the drug deteriorate on keeping. There are also two resins in the root.

Physiological Action.—Although cimicifuga has been most extensively used by American practitioners since the publication of the paper of Dr. Young (*American Journal of the Medical Sciences*, vol. ix.) in 1831, yet we have very little accurate knowledge as to its physiological action. Dr. Chapman (*Elements of Therapeutics*, 6th ed., vol. i.) affirms that in full doses it causes some nausea, more or less relaxation of the surface, vertigo, tremors, and decided reduction of the pulse; and Dr. N. S. Davis (*Transactions of the American Medical Association*, 1848, vol. i. p. 351) dwells very strongly upon its sedative action. In full doses it certainly influences the cerebrum, producing intense headache and giddiness. Although in large doses it vomits, yet its emetic action is never violent, and it never causes more than relaxation of the bowels. Various practitioners have asserted that it acts upon the respiratory mucous membrane.

Therapeutics.—Cimicifuga was originally proposed by Dr. Young as a remedy in *chorea*, and since his time has been very largely used in that disease by American practitioners. In simple chorea, such as exists in children, its value is unquestionable. It must be given freely, and in most cases the consentaneous exhibition of iron and laxatives materially aids in effecting a cure.

In acute *inflammatory rheumatism*, cimicifuga has been highly recommended by Dr. Davis and other practitioners. I have seen it do good, but it is at present very rarely, if ever, used. In *chronic bronchitis* it is sometimes employed with benefit, especially when the expectoration is free and hectic exists.

ADMINISTRATION.—As cimicifuga deteriorates by keeping, the fresh drug should always be used. The powder (dose, twenty grains) is preferred by some practitioners; but I have found the officinal *fluid extract* (*Extractum Cimicifugæ Fluidum*, U. S.) very active in doses of from twenty minims to a fluidrachm. The dose of the *tincture* (*Tinctura Cimicifugæ*—1 to 5, U. S.) is one to two fluidrachms.

CAFFEA—COFFEE.

The seeds of the Caffea Arabica are such familiar objects that space will not be here occupied with their description. It should be remembered that coffee contains, besides *Caffein*, an empyreumatic oil, which has decided effects upon the system.

CAFFEINA. U.S.

Caffeine occurs in long, snow-white, silky, opaque, odorless crystals, sometimes conjoined into feathery crystals, of a feeble bitter taste. It has a neutral reaction, but unites with acids to form salts. It is soluble in 100 parts of water, 160 parts of absolute alcohol, and 220 parts of ether. It was first discovered in coffee by Runge (*Schweigg. Journ. Chem. Phys.*, xxxi.), in 1820. In 1827, Oudry discovered a principle in tea which he called *thein*, which in 1838 was proven by Mulder and C. Jobst to be identical with caffein. Martius, Stenhouse, J. Attfield, and other chemists have also shown that caffein is the active principle of *Guarana* (the fruit and leaves of the *Paullinia sorbilis* of Brazil), of *Maté* or *Paraguay tea* (the leaves of the *Ilex Paraguaiensis*),[*] and of the *Kola nut* of Africa (*Cola acuminata*). H. M. Smith (*Journal of Applied Science*, Sept. 1874) has also found it in *Yaupon* (the leaves of our native *Ilex Cassine*).

PHYSIOLOGICAL ACTION.—The study of the physiological action of caffein in relation to its therapeutic use can be most conveniently made in two divisions, namely, the action of toxic and that of minute doses.

Toxic Doses.—The influence of the alkaloid upon frogs has been studied by Albers (*Deutsches Klinik*, 1853, p. 370), Falck and Stuhlmann (*Virchow's Archiv*, Bd. xii. p. 365), Mitscherlich (*Der Cacao und die Chocolade*, Berlin, 1859), I. Hoppe (*L'Écho Méd.*, 1858), Brill (*Das Kaffein*, Inaug.

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[*] *Maté* is used in South America very largely as a substitute for tea. According to the analyses of Dr. Peckolt, of Rio Janeiro, it contains 2.5 parts in a thousand of caffein; but M. Byanon found 1.85 per cent. of the alkaloid (*Bull. Thérap.*, xciii.). It is sold in two forms: *maté in leaf* is prepared as ordinary tea is, and taken with sugar and milk to taste; *maté in powder* is prepared by pouring upon the powdered maté boiling water, and sucking up through a tube, the bulbous end of which is furnished with a fine sieve, or the powder is thrown into the boiling water, and when the mixture recommences boiling, cold water is poured into it; this precipitates the powder, and the infusion is taken clear.

Diss., Marburg, 1861), Oscar Johannsen (*Ueber die Wirkung des Kaffein*, Inaug. Diss., Dorpat, 1869), and various other observers. The minimum fatal dose is stated by Leven (*Arch. de Physiol.*, 1858) to be .015 grain in a frog of moderate size. According to the various observers, the chief symptoms induced by poisonous doses in the batrachian are muscular quietness and weakness, with disturbance of respiration, succeeded by a stage of violent tetanic convulsions, ending in general paralysis and death by asphyxia, the heart beating after the cessation of respiration, although evidently much affected.

Johannsen denies that there are any true convulsions produced in the frog by caffein, but merely a rigidity, muscular in its origin and very closely allied to that produced by heating a muscle, *i.e.*, to post-mortem rigidity. Pratt, however, previous to the publication of the paper of Johannsen, had very clearly recognized the existence both of this muscular stiffness and of convulsions, and had pointed out the difference between the latter and those of strychnia, differences which are the result of the peculiar condition of the muscles in thein-poisoning. He says, "At the commencement there is the usual rapid action and abrupt contraction of the muscles; but as the phenomena go on, the muscles seem to act sluggishly, requiring quite an interval to contract and relax, . . . the spinal cord having to deal with muscles already much contracted by the local action of the poison on their fibres." Moreover, Leven (*loc. cit.*, p. 182) destroyed entirely the lower third of the spinal cord in a frog, and administered caffein, when the characteristic convulsions appeared in the upper two-thirds of the animal, but not in the lower third.

Pratt included all the tissues of a frog, except the spine, in a tight ligature just above the bifurcation of the aorta, and administered thein, when the anterior legs became very stiff, and had also occasional severe convulsions, in which the hind legs participated, although between the paroxysms they were perfectly relaxed. He also noted in a number of experiments that the hind legs became very rigid, but not convulsed, after the lower portion of the spinal cord had been removed and the animal poisoned.

Buchheim and Eisenmenger (quoted by Schmiedeberg) have recently corroborated the muscular changes noted by Johannsen, but insist, with Pratt, that there are also true nervous convulsions. O. Schmiedeberg (*Archiv für Experim. Pathol. und Pharm.*, Bd. ii.) believes that he has reconciled these differences of observations by finding that the alkaloid acts much more powerfully upon the muscles of Rana temporaria than upon those of R. esculenta; so that a dose of caffein which causes intense general muscular stiffness in the former produces in the latter only true convulsions, the convulsions in R. temporaria being prevented or masked by the disorder of the muscles.

The more recent researches of E. Leblond (*La Caffeine*, Paris, 1883) do not confirm this idea of Schmiedeberg, but show that the differences depend rather upon the size of the dose and variations in the sensitiveness of individual frogs. Johannsen pointed out that the rigidity spreads from muscle to muscle as the hypodermically injected poison diffuses itself, and is never developed in a leg to which access of the poison is denied; whilst Voit found that muscular rigidity came on as usual after severing the nerve of a leg. The rigidity and paralysis are muscular, and the elaborate studies of Leblond appear to prove that there are at least two stages (similar to the phenomena of veratria-poisoning) in the action of caffein upon the frog muscle, one in which the muscular excitability is exaggerated, and in which there is a tendency to prolonged tetanic contractions after even momentary stimulations of muscle, and the final stage of rigidity and lost excitability.

The action of caffein upon the muscle is readily demonstrated by throwing the isolated gastrocnemius of the frog into a one per cent. or even a weaker solution; in from two to three minutes the muscle becomes contracted, swollen, round, stiff, and unable to respond to the galvanic current. That it is the muscle fibre which is affected is shown by the experiments of Pratt and Voit, already quoted, in conjunction with one in which Pratt found that when an isolated muscle was soaked in a solution of curari until the nerves were killed, and then thrown into a solution of caffein, the usual rigidity was developed. Johannsen (*loc. cit.*, p. 22) states that when a muscle under the microscope is touched with caffein, its fibres can be seen to contract half their length.

In birds poisoned with caffein, the symptoms (Brill, *loc. cit.*, p. 66) are irregular movements, apparently to some extent due to cerebral disturbance, increased rapidity and irregularity of respiration, spasmodic tremblings, and tetanic and clonic convulsions, with paralytic phenomena. In mammals the results of the toxæmia, as noted by various observers,[*] are restlessness, hurried respiration, at first a slight lowering and afterwards a decided elevation of temperature[†] (Alex. Bennett), muscular weakness, tetanic and clonic convulsions, increasing general paresis, and finally death, apparently from paralytic arrest of respiration. There is still a good deal of uncertainty as to the nature of the convulsions; but Amory in some not very conclusive experiments found that they did not occur below the point at which he had divided the cord. If this result be correct, the convulsions must be cerebral; but confirmation is lacking. Uspensky (*Reichert's Archiv*, 1868, p. 526) has found that forced artificial respiration in great measure suspends the convulsions.[‡]

Nervous System.—There is no evidence that caffein exerts a very marked influence upon the cerebrum of the frog, or even of some of the lower mammals, unless the convulsions induced by it are believed to be the result of some such action. In certain of the higher animals, such as the cat, it often produces a condition of almost frantic cerebral excitement. The convulsions produced in the frog by caffein seem, however, to be spinal. Both Pratt and Leblond have found that section of the cord high up does not prevent them, so that they are not cerebral; whilst in Pratt's experiments, as well as in those of Leven, destruction of the spine prevented their development. The conclusion seems established that in the frog caffein *acts as a motor spinal stimulant and also as a muscle poison.*

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[*] Leven (*Archives de Physiologie*, 1868; Amory (*Boston Medical and Surgical Journal*, i., 1868); Pratt (*Ibid.*, ii., 1868); Alex. Bennett (*Edinburgh Medical Journal*, Oct. 1873).

[†] Attention has recently been called, especially by Prof. Binz, to the effects of caffein upon animal temperature. He states that minute doses have no effect upon the bodily temperature; doses just enough to produce slight toxic symptoms cause a rise of 0.6° C.; excessive doses an elevation of 1° to 1.5° C., the maximum being reached in one to two hours; doses which rapidly kill have very little effect upon the temperature (*Arch. Exper. Path. u. Therap.*, ix. 31).

[‡] In an elaborate series of experiments, Dr. Bennett (*British Medical Journal*, 1874) found that the minimum fatal dose of the poison for the cat and the rabbit was a little over a grain for the pound, five and a half grains being required for a five-pound animal.

Alex. Bennett has brought forward the theory (*loc. cit.*, and *British Medical Journal*, 1874) that caffein paralyzes the posterior columns of the cord without affecting the anterior columns; but his evidence appears to me insufficient to prove his conclusions. He grounds his belief chiefly on finding that in poisoned frogs and rabbits galvanization of the posterior columns of the exposed cord produced either no muscular contractions or only such as were very much more feeble than those provoked by galvanization of the posterior columns.

The motor nerves appear not to be affected, since Alex. Bennett has found that after death from thein they retain their normal susceptibility, and Pratt surrounded one crural nerve of a frog with a paste "of thein and water," and irritated the spinal cord, when both legs responded with uniform alacrity. Bennett also tied the crural artery of a frog, poisoned it with the alkaloid, and found that irritation of the cord produced equally active contractions in the two legs. Upon the sensory nerves it is affirmed that the poison acts more decidedly; but careful experiments are still wanting to prove this. The chief evidence is furnished by Pratt, who found that when the left sciatic nerve of a beheaded frog was surrounded by a paste of thein and water, after ten minutes irritation of the right foot produced reflex movements, whilst irritation of the left foot failed to elicit any response. Leblond has noted marked hyperæsthesia in the frog, and Rumpf affirms (*Schmidt's Jahrb.*, Bd. cci. p. 123) that increased sensibility of the skin can be demonstrated in man.

Circulation.—The action of caffein upon the circulation has not been sufficiently studied to enable us to reach definite conclusions. It can hardly be doubted but that it has a direct influence upon the heart, although that viscus continues to beat in animals poisoned by the drug after the cessation of respiration. According to Voit (quoted by Brill), in the frog the rapidity of the cardiac pulsation is at first increased, but the pulsations become slower and slower, and are accompanied by irregularity of rhythm, the heart finally ceasing to act, but still responding to stimuli at a time when the voluntary muscles are absolutely dead. Falk, Steehlmann, and Johannsen observed that caffein first increases and then lessens the frequency of the cardiac pulsations in the frog. According to Johannsen, the lessening of the frequency comes on the more quickly and the more powerfully as the size of the dose is increased. After a time the heart begins to beat irregularly, with short intermissions, which, as time goes on, grow longer and longer, and at last movement ceases. Johannsen found the action upon the cut-out frog's heart was the same upon the viscus *in situ;* Leblond confirms this, and states that the heart is finally arrested in systole; also Dr. Thos. I. Mays (*Therap. Gaz.*, i. 1885, 84).

Aubert and Haase (*Pflüger's Archiv*, v. p. 608) find that the action of the alkaloid upon the pulsations of the frog's heart varies greatly, and indeed the individual experiments of the authors previously quoted show such variation. This is confirmed by the research of Dr. Rioschiro Maki (*Ueber den Einfluss des Camphers, Caffeins und Alkohols auf das Herz*, Strassburg, 1884). This investigator experimented upon the cut-out frog's heart with the Williams apparatus, and found that the pulse was variously affected. In most of his experiments, the arterial pressure—*i. e.*, the heart's work—was markedly lessened, but in a few cases it was distinctly increased. It would seem probable that small doses of the alkaloid stimulated the frog's heart and large ones depressed it.

Upon the heart of the mammal, so far as can be judged from the present evidences, caffein acts more powerfully than upon that of the frog Leven found that in the first stages of the toxæmia both the pulse-rate and the arterial pressure are markedly increased. In a series of experiments upon dogs, Aubert (*Pflüger's Archiv*, v. p. 612) found as an almost constant effect that the drug produced an increase in the pulse-rate with a marked lessening in the height of the pulse-wave. There was also marked fall of the arterial pressure, which, with the small pulse-wave, Aubert believed to be the result of the direct action of the drug upon the heart-walls themselves. These experiments were made with very large amounts of the alkaloid injected into the jugular vein; in most cases, the animal being kept alive by artificial respiration. In one experiment there was a very distinct rise of the arterial pressure (*loc. cit.*, p. 615).

Prof. Binz (*Arch. f. Exper. Path. u. Pharm.*, ix. 36) made two experiments upon dogs: in one of them, the alkaloid was given after section of the vagus. In each case there was a very distinct rise of the arterial pressure. Maki made a number of experiments, and found that large doses were followed by a distinct fall of the arterial pressure. In most cases he failed to obtain a first rise of the arterial pressure; but as his experiments were made upon animals that had been chloralized or atropinized, they were of comparatively little value. Aubert (*loc. cit.*, p. 617–18) found that after section of the vagi the frequency of the pulse was still increased by caffein, and that galvanization of the nerve failed to arrest the heart's action. The most important evidence indicative of a stimulant effect upon the heart is furnished by Leven (*loc. cit.*, p. 184), who asserts that after he had divided the pneumogastrics and sympathetics, and isolated the heart from all connection with the nerve-centres, an administration of caffein increased both the heart-pressure and the pulse-rate.

This summary comprises all the experimental evidence that we have in regard to the action of caffein upon the circulation. It is very evident that at present no positive conclusions can be reached, and that further researches are imperatively demanded.

The only case of poisoning by caffein I have met with is reported by Dr. C. H. F. Routh (*London Lancet*, 1883, i. 680). An adult took a drachm of the pure citrate. The symptoms developed at once; they were burning in the throat, giddiness, faintness, nausea, numbness, and tremors of extremities, pain in stomach and bowels, profuse diuresis, and finally collapse, with great cardiac oppression and icy extremities. Consciousness was not impaired, and there was no headache until the patient began to recover.

In a case reported by Dr. Curschmann (*Deutsche Klinik*, 1873, 377), a woman, in order to produce an abortion, took a decoction made from about eight ounces of freshly roasted coffee. Two hours later she was found in a condition of great anxiety, with a sensation of intense need for air; was exceedingly restless, and continually attempted to get up from her chair, but was powerless to do so. All the extremities, but especially the hands, were affected with very pronounced choreic tremors. She knew persons and her surroundings, but her cerebration was very much affected, and the next day she remembered nothing that had happened at this time. The respiration was quick, twenty-four and twenty-five per minute, and short. The pulse one hundred and twelve; the heart-beats very strong, even violent. One hour after the ingestion of the dose violent diarrhœa set in and continued until the next day. The passages were very thin and watery, with but little violent pain but much tenesmus. There was also marked tenesmus of the bladder. The urine was greatly increased in quantity, with specific gravity of 1014.

Effects of Therapeutic Doses.—The peculiar wakefulness, the increased mental activity, and the often nervous restlessness which are induced by strong coffee are familiar phenomena to almost every one. They are without doubt largely, but are not altogether, due to the caffein contained in the beverage. By doses of two or three grains of the alkaloid a very similar state of body and mind is induced. Lehmann found that eight grains of caffein produced increased frequency of the pulse, very frequent urination, tremulousness, excited mental action, passing into a form of delirium, with confusion of thought, visions, and finally a deep sleep. The largest amount that I have met with as having been taken by man (twelve grains) was ingested by Dr. Pratt (*loc. cit.*). About two hours after the dose had been swallowed, intense physical restlessness and a very uneasy condition of the mind were developed; very marked general muscular tremulousness soon followed, and the mental anxiety increased. After this passed off, there was obstinate sleeplessness, with active and persistent thinking, and frequent urination. The increase of brain-power which has been noticed by various observers after caffein, as well as after coffee, tea, guarana, and all the allied crude drugs, is undoubtedly real, and must be due to a direct stimulant action exerted upon the cerebrum. The experiments made upon animals with toxic doses indicate very strongly that the physical restlessness and tremulousness are due to spinal stimulation and are the counterpart of the convulsions which toxic doses produce.

It appears to me that the cerebral stimulation of caffein differs from that of opium in that it affects the reasoning faculties at least as profoundly as it does the imagination. Coffee prepares for active work both mental and physical, opium rather for the reveries and dreams of the poet.

The enormous use made by mankind of substances containing caffein indicates that in some way it is directly of service in the wear and tear of daily life. It is not probable that any of the caffein is assimilated, but it is thought by some authorities to check very greatly the elimination of nitrogen, or, in other words, lessen the waste of tissue. The subject was laboriously investigated by Julius Lehmann in 1853, and by F. W. Böcker in 1854, and earlier. Dr. Lehmann found that the exhibition of six grains of caffein daily, the regulated diet being uniform, diminished the elimination of urea from twelve to twenty per cent. Upon experimenting with the empyreumatic oil of coffee he found that it lessened even to a proportionately greater extent the elimination of urea, and also acted very powerfully in producing sleeplessness, so that the favorite beverage is by no means dependent upon its contained caffein for all of its activity. Dr. Böcker published his researches on coffee in 1849 (*Beiträge zur Heilkunde*, Bd. i.), but I have never seen any abstract of the article, other than the statement that he found that the drug causes diminished elimination of urea. His investigation of the effect of tea was most elaborate and laborious (*Archiv der Vereins für Gemeins. Arbeiten z. Förderung d. Wissen. Heilkunde*, Bd. i. p. 213). He analyzed the fæces, the urine, and the products of respiration, and found, a similar diet being maintained, that the tea did not affect sensibly the elimination of carbonic acid from the lungs, but did very decidedly diminish the excretion of urea, and also of nitrogenous matters in the fæces. He then tried abstaining from food for periods of thirty-six hours, with and without the use of tea, with results perfectly in accord with those just stated. The results obtained by various experimenters are singularly at discord. Henri Hoppe (*Deutsches Klinik*, 1857), in experiments upon a dog, found that coffee diminishes very slightly the urea elimination, but greatly increases the output of carbonic acid. In regard to urea, Rabuteau and his pupil Eurastratiade, working with coffee upon men and dogs, obtained results similar to those of Böcker (*Compt. Rendu*, 1870, lxxi. 426, 732), as did also Hammond in this country. On the other hand, C. G. Lehmann (*Lehrb. d. Physiolog. Chemie*, Bd. i., Leipsic, 1842), Voit (*Untersuchungen*, Munich, 1860), and Roux (*Arch. Physiolog. Norm. et Path.*, 1874, i. 592) found that caffein or coffee sensibly increase the elimination of urea, or, in those accustomed to the daily use of coffee, have no influence.

In a long series of experiments upon dogs by MM. Couty, Guimaraes, and Niobey, it is affirmed as a uniform result that the use and assimilation of nitrogenous food was greatly increased, that the carbonic acid and oxygen in the blood were markedly decreased, and that the proportion of sugar and of urea in the blood was notably increased (*Compt.-Rend. Soc. Biolog.*, v. 546; *Compt.-Rend. de l'Acad.*, xcix. 86).

In the present state of the evidence a positive conclusion can scarcely be reached, but I am strongly inclined to believe that the habitual use of moderate amounts of tea or coffee has practically no effect upon tissue-waste.

Elimination.—According to the experiments of Richard Schneider (*Ueber des Schicksal des Caffeins*, etc., Dorpat, 1884), caffein, when taken in therapeutic doses, is entirely destroyed in the system, and when in toxic amount, is partially destroyed and partially eliminated by the kidneys.

THERAPEUTICS.—The use of caffein as a remedial agent in disease is very limited, whilst its employment in health as an article of diet is the daily practice of a great part of the race. The chief indication in disease which our knowledge of the physiological action of the drug establishes its fitness to meet, is as a cerebral stimulant; for this purpose it is often used in *nervous headaches* and in *opium-poisoning.* The first of these disorders it sometimes relieves in a marvellous manner, but more often it fails to accomplish good. To predict in any case what its influence will be, in the present state of our clinical knowledge, is impossible; but the remedy may always be tried in safety in the dose of two grains, taken when the paroxysm is coming on, and repeated once in forty minutes if necessary. Very strong coffee is almost always administered in unlimited quantities in opium-poisoning, but, so far as I know, Dr. J. Hughes Bennett (*British Med. Journ.*, 1874, p. 697) has made the only attempt to establish by exact experiments the asserted antagonism of caffein and opium. That observer found that the exhibition of from four to four and a half grains of caffein would save a proportion of cats poisoned with the previously-ascertained minimum lethal dose (1⅞ gr.) of morphia. Several of the cats which had thus been saved succumbed some days afterwards to one and seven-eighths grains of morphia. The caffein was powerless to save animals to which larger doses of the narcotic had been given: so that it is fair to conclude that caffein is within narrow limits antagonistic to the narcotic alkaloid.

There is at present much evidence to show that caffein is a cardiac stimulant. Its action upon animals has been already discussed, and both Leblond and Prof. F. Riegel (*Berlin. Klin. Wochens.*, xxi. 1884) are in accord in affirming that given to healthy men it decreases the rate, and markedly increases the force of the pulse. It has been largely used by Prof. Riegel and by Dr. C. Becker (*Wien. Med. Bl.*, vii. 21), as a substitute for digitalis in cardiac disease with asserted very good results. It is even preferred to digitalis, because it acts more promptly and is free from cumulative action. Dr. Becker gives from eight to thirty grains of the pure citrate in divided doses during the twenty-four hours, beginning with the smaller quantity, and rapidly increasing until the result is achieved. I have myself seen very good results from it in weak heart. The statements of Prof. Gubler (*Bull. Thérap.*, xci. 513) that the citrate of caffein is a powerful diuretic have received strong confirmation (see *Lond. Practitioner*, xxii., xxiv., xxv.). It may be used in *cardiac dropsy*, and in *chronic Bright's disease* in doses of three grains every three or five hours. In *acute Bright's disease*, it should be employed with caution, if at all. It is said that most of the salts of caffein are decomposed in the presence of water, and are, therefore, ineligible for hypodermic use; the double benzoate of sodium and caffein has been proposed as moderately stable and free from irritant properties. One equivalent of salicylate of sodium (160) will also cause the solution of one equivalent of caffein (244), and the following formula has been commended by M. Tanret for hypodermic use: Sodii salicyl., 31 gr.; Caffein, 40 gr.; Aqua destillat., 60 gr.

ERYTHROXYLON—COCA. U.S.

The leaves of the Erythroxylon Coca, a South American shrub, which is very largely cultivated in Peru and neighboring countries, resemble in size and shape those of the tea, but are not dentate, and are distinguished from most medicinal leaves by a slightly curved line, running from the base to the apex, on each side of midrib, and produced by the peculiar folding of the leaf in the bud. In 1855, Gardeke discovered in coca an alkaloid to which he gave the name *Erythroxyline*; but this principle was first thoroughly studied by Dr. Albert Niemann, from whom it received the name *cocaine*, by which it is now usually known. It occurs in colorless, transparent prisms, soluble in seven hundred and four parts of cold water, and forms with the acids very bitter, soluble, crystallizable salts; besides it, the leaves contain a peculiar tannin, known as *coca-tannic acid*.

Physiological Action.—From the days of the Incas the leaves of the coca plant have been enormously used by the natives of Western South America as a stimulant, and it is stated that about forty million pounds of them are annually harvested. Mixed with ashes or a little lime they are chewed, and are said to greatly increase for the time being the muscular strength and endurance. Although coca is thus employed habitually, our knowledge of its action upon the human organism is very incomplete, and but few scientific observers have given detailed reports of the symptoms it causes. There can be no doubt that moderate doses temporarily increase, to a very extraordinary degree, both physical and mental power. The most important account of its action upon the human being that we have is that of M. Montegazza, but all investigators concur in praising the peculiar sense of calm and happiness, the insensibility to fatigue, and the increase of bodily and mental activity which the drug produces.

Montegazza states that when he took two hundred grains of the leaves, he was in a short time plunged into a condition of peculiar physical beatitude, in which he seemed to be isolated from the rest of the world, and to live in a peculiar atmosphere of active calm. In a little while there came also a sense of plenitude of power, which was accompanied by a real increase of physical ability, so that gymnastics, which in his ordinary condition were impossible to him, became easy. This state was succeeded by a natural profound sleep, lasting sometimes the whole of twenty-four hours. After very large doses of coca, in Dr. Montegazza's case, a peculiar series of symptoms occurred to which the name of "cocaleine intoxication" was given. Thus on one occasion he took thirty-five grammes, and an hour later nine grammes, etc., until he had taken in the course of two hours sixty grammes in all. The heart, which after the earliest dose had been slow in its actions, directly after the second dose suddenly became rapid and very violent in its beats; but at the end of the two hours the palpitations had ceased, although the pulse was still one hundred and twenty-eight per minute. There was now a condition of intoxication similar to that which is produced by hasheesh. M. Montegazza was possessed by a feeling of intense beatitude and inner joyousness, whilst a succession of visions and phantasmagoria, most brilliant in color and form, trooped rapidly before his eyes. He seemed to himself to look upon a world of shifting and incessant activity, as into a kaleidoscope. He rapidly passed into a delirious condition, in which he appeared to himself to be unconscious, although when addressed he would answer rationally. To his own consciousness he was, as it were, buried in a revery, or perhaps a more accurate description would be to say that he felt as though, by a sudden rush of intellectual and emotional life, he was carried out of himself, and knew not whether he was in or out of the body. An hour or two later he was sufficiently calm to say to his friends "that God was unjust, in that he had made man to live without eating coca. I prefer a life of ten years of coca to one of a thousand years without it." As this state was passing off he was seized with an irresistible desire to reproduce its delirium by taking more coca. Finally, however, he fell into a condition of sleep, which lasted only three hours. After this he was able to resume at once his ordinary occupations, and offered no physical evidences of his coca debauch.

The moderate daily use of coca, according to our best information, is not injurious, and increases the working powers; but, according to Prof. Poeppig, the habit of the excessive use is readily formed, and produces very serious results. The first symptoms are usually those of disorder of the digestive organs. Little by little the power of digestion is lost; an incurable insomnia is developed, emaciation becomes extreme, ascites appears, and the patient finally dies in a condition of general marasmus. Other authors especially dwell upon the enfeeblement of the intellectual faculties as very marked in those who use the stimulant to excess. Dr. Tschudy states that the inveterate coca-chewer can be recognized by his uncertain step, his general apathy, his sunken eyes surrounded by a deep purple aureole, his trembling lips, green encrusted teeth, and his excessively fetid breath, with the peculiar blackness about the corner of the mouth.

Pronounced aphrodisiac properties have been attributed to coca, but they seem to rest rather upon tradition than demonstrated experience. According to M. Unanue, the ancient inhabitants of Peru represented Venus by a female figure with a coca-leaf in her hand, and the coca still plays an important part in the nuptials of the Indians.

It has been affirmed by Tschudy and Unanue that coca is able to take the place of food, but this is clearly not the case. Dr. Weddell himself states that although an Indian chewing the coca could go on foot many hours without fatigue and without food, yet at the end he would eat more at one repast than he himself would take in two days. He accords with Bibra (*Die Narkot. Genussmitell*, 1855) in stating that the coca has the power of putting aside for some time the sense of hunger. Whilst, however, it may mask the appetite, it certainly does not nourish the body. Thomas Moreno y Maiz (*Thèse*, Paris, 1868) made several crucial experiments by keeping animals in pairs without food, and giving to one coca freely. These experiments have been repeated by B. von Anrep (*Pflüger's Archiv*, 21, 1880), and in every case the animal which received the coca died at least as early as its mate.

In order to cause death enormous doses of the alkaloid cocaine would be required. According to Von Ploss (quoted by Husemann, *Die Pflanzenstoffe*' 2d ed.), an apothecary for suicidal purposes took twenty-two grains of cocaine in a glass of beer. He shortly afterwards went to sleep, but awoke in some hours with great abdominal pains, dryness in mouth, excessive weakness, and vertigo. He suffered from suppression of urine for twenty-four hours, but had no further disturbance of consciousness or of the heart's action.

Besides the studies of Dr. Ott (*Toxicological Studies*, Philadelphia, 1874) there are three physiological articles upon coca. Two of these memoirs I have never seen, and only know them through abstracts, especially those in the article of B. von Anrep (*Archiv fur die Gesammte Physiologie*, Bd. 21, 1880, page 38). With this material it is possible to examine somewhat in detail the physiological action of the drug.

It may in the first place be considered settled that very small doses (one to three one-hundredths of a grain of cocaine) produce in the frog no other symptoms than some evidences of excitement. After doses of from one-tenth to one-fiftieth of a grain the frog becomes quiet, with an apparent increase, however, in the reflex activity, sometimes amounting to tetanus, followed by increasing palsy and failure of the respiration; very large doses produce symptoms of paralysis.

In the domestic animals the symptoms vary. In the rabbit, there is first a peculiar state of quiet, followed in a few moments by a condition of great excitement, in which the animal springs and jumps about. A few minutes later the rabbit again becomes quiet, and now, although trembling much, is so weak that he moves with difficulty. The tremblings increase until they merge in convulsive movements of the legs, whilst at the same time there is partial paraplegia; pendulum movements of the head are very marked, and finally epileptiform convulsions appear, whilst at the same time a peculiar tetanic rigidity seems to indicate spinal excitement. The lethal dose for a rabbit is put at a grain and a half per kilo. Dogs and cats are said to be more susceptible to the action of cocaine than is the rabbit, and to suffer similar symptoms, but especially with the dog the evidences of mental excitement are more pronounced.

Nervous System.—The most susceptible portion of the body to the action of the cocaine is the cerebrum. The peculiar sense of calm which follows moderate doses of the drug is evidently the result of the action on the brain, which eventuates, after a sufficient dose, in the peculiar ecstasy so graphically described by Montegazza. According to the description of Von Anrep, this delirium is almost equally pronounced in the dog; thus a very quiet animal, almost immediately after the injection of the cocaine, will begin to dance and leap, never standing still for a moment, and continually circling around the experimenter. The movements are not at all those of convulsions, but voluntary, and accompanied by every expression of joy and exhilaration. This may continue for hours, and the animal become gradually quiet, and pass finally into his normal condition. If instead of a moderate dose a toxic one has been given, there is first a period in which the animal is very restless, but seems full of terror and anxiety; the least sound frightens him, causing him to tremble and to drop his tail between his legs. He does not appear at this time to know his master. Rhythmical movements of almost all portions of the body accompany this state. Fifteen or twenty minutes later the mental condition alters, and the dog becomes apparently full of joyous excitement. He barks loudly, runs from one person to another licking them, and giving all the characteristic signs of joy and pleasure. After a few moments this condition gives way to one of increasing feebleness; the dog gradually gets unable to move, rhythmical movements, cramps, and convulsive symptoms appear; the pendulum-like movements of the head become very violent, and at last narcosis develops. It is evident that many of these symptoms are psychical.

B. von Anrep believes that the drug has a very distinct and peculiar influence upon the *semicircular canals*, thereby causing the peculiar pendulum-like motions of the head, the lack of co-ordination, and the rolling convulsions especially seen in doves.

According to the researches of Von Anrep, the convulsive movements are of cerebral origin, and are arrested by section of the spinal cord. Dannini appears, however, to have found that the section of the cord did not prevent convulsions in the hind feet. To settle this discrepancy further experiments are of course necessary. It is to be remarked that even Von Anrep affirms that after, as before, section of the spinal cord reflex activity is increased by cocaine, and certainly other observers have noticed an increased reflex activity as constant after small doses. This evidence indicates that the drug stimulates the spinal cord; yet it is possible that sensory stimulation may be the sole cause of the excited reflex action.

It is established by the concord of almost all observers that the *sensory nerves*, after sufficient doses of cocaine, are finally paralyzed. The statements and experiments of Nikolsky, of B. von Anrep, and also of Ott, appear to prove that the paralysis is preceded by increased functional activity.

The *motor nerves*, according to Dannini, in the frog remain irritable until after death; but, according to Nikolsky, their functional activity is first increased and afterwards destroyed. Ott also asserts that cocaine depresses the motor nerves, and Moreno y Maiz found that when he tied the iliac artery of a frog on one side and administered cocaine anteriorly, there came a time when irritation of the poisoned limb caused no movement, whilst irritation of the protected extremity provoked very distinct general reflexes. At the same time there was diminished motility in the non-protected limb as compared with the protected one. These facts of course indicate that the drug finally depresses both motor and sensory fibres, but that its action upon the motor is subordinate to that upon the sensory nerves. Ott also noticed that there is a time in the poisoning when irritation of the central end of a cut sciatic nerve produces no response, whilst irritation of its peripheral end causes muscular action, and thereby confirms the view that the drug affects the sensory earlier and more powerfully than the motor nerves.

An observation made at a certain stage of the poisoning by Dr. Ott—viz., that irritation of the posterior columns of the spinal cord produces no effect, whilst a prick of the anterior column is followed by the usual result—shows that there is the same difference in action upon the sensory and motor tracts of the cord as upon the corresponding nerve-trunks. Indeed, B. von Anrep (*loc. cit.*, p. 56) found that after tying one of the arteries and administering cocaine, the protected leg soon lost the power of reflex action,—evidence that the sensory side of the cord is only somewhat less susceptible to the influence of the alkaloid than are the sensory nerves themselves.

Circulation.—According to Von Anrep, as well as the earlier observations of Nikolsky, the heart of the cocainized frog is gradually weakened and arrested in diastole; but observers agree that, except after enormous doses of cocaine, the heart remains beating long after cessation of respiration.

In mammals, according to B. von Anrep, the pulse-rate is usually increased by full doses of the alkaloid. B. von Anrep states, however, that this increased rapidity is not marked in rabbits, and in Ott's experiments upon dogs before death the pulse usually becomes slower. It certainly was not constant. In regard to the action of cocaine upon the vagi there is an absolute contradiction of evidence. Anrep affirms that these nerves are paralyzed by large doses, and that this condition is never preceded by excitement, whilst both Ott and Nikolsky state that cocaine does not affect the vagi at all. Whatever may be the action of cocaine upon the heart, it seems established that the rise of arterial pressure which it causes is largely the result of contraction of the arterials produced by stimulation of the vaso-motor centre in the medulla; since Dannini has found that after section of the cord cocaine is powerless to increase the arterial pressure, and Ott, that when the cord is cut in the cocainized dog the pressure falls to the level it usually occupies after such section in the unpoisoned animal.

Muscles.—There is a distinct contradiction as to the effect of cocaine upon the striated muscles. Both Nikolsky and B. von Anrep state that the latter are not affected by the alkaloid, whilst Ott affirms that it acts upon them like veratria, and is confirmed in this by Buchheim and Eisenmenger (*Pflanzenstoffe*, 2, p. 885). The tracings given by Ott would appear to prove that the muscular contraction is prolonged by cocaine, and can hardly be accounted for by a condition which M. J. Rossbach and B. von Anrep (*Pflüger's Archiv*, Bd. xxi. 243) allege to be produced, viz.: a peculiar extensibility of the muscle similar to that produced by curari, and like it caused by a lessening of muscle tonus by paralysis of the peripheral nerve endings.

Temperature.—Observers agree that there is during a certain stage of cocaleine intoxication a remarkable rise in the rectal temperature. According to Bennett, Ott, and Von Anrep, this rise of temperature is preceded by a fall; in toxic cases the temperature appears again to become subnormal before death. Von Anrep states that the skin temperature is always elevated from the beginning. The rise in the rectal temperature reaches the maximum (1° C.) during the convulsive stage, but is not produced by the convulsions, as Dannini has found that it occurs in curarized animals.

Elimination.—According to Moreno y Maiz, cocaine is eliminated by the kidneys. Tarchanoff has noticed sugar in the urine after poisoning; but Anrep affirms that the sugar and the albumen, which is also frequently present, are caused by the asphyxia.

Both Dr. Ott and Atherton P. Mason (*Boston Med. and Surg. Journal*, Sept. 1882) find that coca lessens the secretion of urine and very markedly the elimination of urea. Dr. Mason employed very large doses of coca during prolonged exercise. It is therefore very probable that this drug diminishes tissue-waste, although Dr. Mason states that Gazeau has obtained contrary results. In Dr. Ott's experiments the urine became filled with crystals of oxalate of calcium.

Respiration.—Fatal doses of cocaine kill by paralysis of the respiration. After small doses, according to Von Anrep, the respirations become somewhat more rapid and deep, or in some cases simply more rapid. After large doses, the respirations become at first rapid and more shallow, then irregular with interruptions, after each of which the respiratory movements begin deep and slow, but become more rapid and shallow until the next standstill.

Intestines.—According to Von Anrep, the intestinal peristalsis is markedly increased by moderate doses. After large doses this increase is followed by great sluggishness deepening into paralysis. Tarchanoff states that coca increases the mucous secretions, but Anrep affirms that it decreases them.

Eye.—The pupil is dilated in both warm- and cold-blooded animals. Nikolsky concludes that this dilatation is not produced by irritation of the sympathetic nerve, because after section of the nerve cocaine still dilates the pupil, and also when the pupil has already been dilated section of the sympathetic does not produce contraction. These facts, however, do not warrant Nikolsky's conclusions, for the action of the cocaine is evidently upon the peripheral nerve endings, since its local application produces a dilatation of the pupil lasting from one hour to two days according to the dose used. The dilatation appears never to be as complete as that caused by atropine, and the power of accommodation, while distinctly lessened in its range, is never entirely paralyzed (H. Knapp, *Cocaine*, New York, 1885.)

Local Action.—Locally applied, cocaine acts as a very distinct and certain anæsthetic, as was noted by Moreno y Maiz in 1862, and by Von Anrep in 1880, although it was not until September, 1884 (*Wien. Med. Wochensch.*, Nov. 1884), that Dr. Karl Koller demonstrated the practical value of the drug. According to the observations of Von Anrep, the nerves of special sense are as readily affected as those of common sensibility; thus cocaine placed upon the tongue abolishes at the place of contact, for the time being, the sense of taste. At the point of contact there is at first marked pallor, but after a short time very pronounced redness. The primary pallor is alleged to be due to a most powerful constriction of the small blood-vessels, and has led Dr. F. H. Bosworth to the conclusion that cocaine produces *rigid contraction in unstriped muscular fibres* whenever it comes in contact with them (*N. York Med. Record*, Nov. 15, 1884). This conclusion is at present probable but not proven.

Therapeutics.—Cocaine appears to act with certainty as a local anæsthetic whenever it can reach the nerve-filaments in sufficient concentration. The skin will not allow it to pass, whilst the conjunctival and nasal mucous membranes are very permeable, and those of the larynx, throat, and vagina are penetrated with more and more difficulty, in the order of their naming. Even in disease of the eye, when a deep operation is to be performed, such as enucleation, either the alkaloid should be injected subcutaneously, or else the solution of the anæsthetic must be reapplied at various stages of the operation. To the nasal surgeon the alkaloid appears to be invaluable, whilst the gynecologist finds it less serviceable, but even he is, by its careful use, able to perform many operations without pain. In painful ulcers, fissures of the anus, etc., its application will afford temporary relief. It is affirmed by many observers that excessive pain is apt to be felt when the anæsthetic effect is going off, and that this, in many cases, overbalances the first relief. It is probable that this pain is the result of the congestion, as Dr. Carl Seiler tells me that after nasal cauterizations this after-pain can be at once arrested by incising the part slightly so as to cause a local bleeding. The congestion which follows cocaine-anæsthesia cannot at present be explained, but, under certain circumstances, is of very great importance, and Prof. P. D. Keyser (*Therap. Gaz.*, Jan. 1885) reports a number of cases of very severe inflammations in the eyeball, after operations in which cocaine had been used, and gives good reason for believing that the cocaine was the cause of very serious results. He condemns its use whenever the eyeball is to be penetrated. The injection of a four per cent. solution of cocaine into the nostrils will, it is affirmed, give immediate relief in acute *coryza*, and trials of the remedy should be made in inflamed *hemorrhoids*, *boils*, and other painful affections. It should especially be tried in *hay-fever*.

Dr. F. H. Bosworth claims that cocaine is not only extraordinarily efficacious as a *hemostatic* in various surgical cases, but that topically applied it will so constringe the blood-vessels of an acutely inflamed mucous membrane as to arrest the disease. In *bronchitis* he applies by means of atomization, using a two per cent. solution, and also putting the solution freely on the nose and throat. Dr. Bosworth affirms that the effects of cocaine upon mucous membranes last for many hours,—a statement hard to reconcile with the general testimony as to the brevity of the primary bleaching. He states that failure often comes from a lack of a proper application.

Drs. R. J. Hall and Halsted (*N. Y. Med. Journ.*, Dec. 6, 1884) have made the very important observation that injecting a solution into a nerve-trunk paralyzes sensation over the whole distribution of the nerve for about twenty-five minutes. In some case advantage may be taken of this. They used as much as thirty-two minims of a four per cent. solution; but this produced severe constitutional disturbance, such as great giddiness, severe nausea, staggering, cold perspiration, etc.

For local use a four per cent. solution may be employed, and when the part is not readily permeable, as in the vagina, it should be thoroughly re-applied once or twice at intervals of five minutes.

The use of coca in internal medicine is at present entirely tentative. It will probably be found advantageous in *neurasthenia*, *melancholia*, *hysteria*, and as a general nervous tonic and stimulant in acute and chronic diseases with exhaustion. It has been commended in Europe in serous *diarrhœas*. It will probably come into use as a means of sustaining men under severe exertion. There is considerable testimony to show that cocaine is of great service in giving relief to opium-eaters after the abandonment of the narcotic.

The best preparation of coca for internal use is the fluid extract, the dose of which is half to two fluidrachms. The muriate of cocaine was used with great alleged success as a stimulant to soldiers making forced marches by Dr. Aschenbraidt (*Deutsch. Med. Wochens.*, ix. 50, 1883). He gave it in doses 0.15 grain, repeated in an hour if necessary. It is probable that one grain will prove to be a moderate dose. Mr. E. Caudwell has taken five grains, with the production of symptoms severe, but lasting not more than two hours (*Brit. Med. Journ.*, i. 1885, p. 17).

CLASS VI.—ANALGESICS.

In the class *Analgesics*, in this work, are placed those drugs whose chief clinical use is in the relief of pain. Of course the *Anæsthetics* might also be discussed under this heading, but, as they make a very marked group of themselves, they are best considered as a separate class. The only drug, besides opium, which seems worthy of a place in the present division, is cannabis indica.

OPIUM. U.S.

The inspissated juice of the unripe capsules of the Papaver somniferum, or poppy. It is obtained by incising the capsules with a small, sharp knife, and twenty-four hours afterwards scraping off the exuded juice with a blunt blade. Opium is produced in various parts of the world,—chiefly in Turkey, Asia Minor, Persia, and India, but also to a very slight extent in England, Germany, and the United States. Our market is almost exclusively supplied from Asia Minor, with the variety known as *Smyrna* or *Turkey Opium*. This occurs in masses from the size of the fist to that of a child's head, irregularly globular, more or less flattened, covered externally with the capsules of a species of Rumex or dock, hard externally, softer and of a reddish-brown color within, and of a strong narcotic odor and taste.

Smyrna opium is at times variously adulterated with gum, licorice, and other substances. Such specimens are said generally to want the Rumex capsules. A rough but pretty fair test of the purity of opium is performed by drawing a piece of it across a sheet of white paper. If it be much adulterated, the mark will be continuous,—not interrupted, as it should be. Often the black color, the adhesive consistency, and the sweetish taste will also betray the nature of the sample.

On exposure to the air, opium becomes hard and brittle, and is readily reduced to a powder of a yellowish-brown color. It yields to water, alcohol, and diluted acids, forming dark-brown solutions. Ether does not extract all of its medicinal principles. It is a very complex body, containing the alkaloids morphia, codeia, narceia, narcotina, thebaia, papaverina, porphyroxia, cryptopia, meconia, opiania, paramorphia, besides meconic, thebolactic, and sulphuric acids, extractive matter, gum, glucose, fixed oils, a volatile odorous principle, and other substances of no importance. In regard to the proportions of the more important principles, Messrs. Smith of Edinburgh obtained from 100 parts of fine opium 10 parts of morphia, 6 of narcotina, 1 of papaverina, 0.15 of thebaia, 0.03 of codeia, 0.01 of meconia, 0.02 of narceia, and 4 of meconic acid (*Pharm. Journ. and Trans.*, October, 1865, p. 183). Good opium should yield from nine to fourteen per cent. of morphia.

As meconic acid strikes a blood-red color with a persalt of iron, the latter affords a ready, although not decisive, test for opium and the meconates.

PHYSIOLOGICAL ACTION.—When opium is taken in such dose as to produce its mildest physiological effects, it exerts a quieting influence, inducing a peculiar dreamy condition,—very generally a feeling of *bienfaisance*,—during which images and ideas float before the mind, and by their endless and effortless repetition shorten the time, which seems to lose itself in rest. It is commonly asserted that there is a stage of the action of opium in which the activity of the mental faculties is exalted. This may be so in some persons, and especially in those who have accustomed themselves to the use of the drug as a stimulant; but my experience is that in those who do not habitually take opium true mental power is, during all the stages of the action of the drug, diminished rather than increased. The state induced is rather the fabled calm of the lotus-eater than the energetic activity of production. Even in those who are accustomed to the use of opium as an aid to work, I think it is the imagination rather than the reasoning faculties which is excited by it. After a length of time, varying according to the idiosyncrasies of the patient and the dose of the drug, the condition which has been noted gradually passes into sleep,—either light and dreamful, or natural, or heavy and deepening into stupor, according to the amount of the drug ingested. On awakening, the patient may return at once to his normal condition, but very often he experiences a state of depression, as shown by languor, a little headache, nausea, or even vomiting, which may last for some hours.

After very large doses, the first stage of the action of opium is very short, or it may be entirely wanting, sleep coming on almost at once. Thus, I have seen deep coma produced in three minutes by a hypodermic injection of morphia. The symptoms of the second stage of opium-poisoning closely resemble those of congestion of the brain: the pupils are strongly contracted the face more or less suffused, often deeply cyanosed; the pulse full, slow and strong; the skin generally dry and warm; the respiration slow and deep, and, it may be, stertorous; unconsciousness is apparently complete, but very generally the subject can be aroused by violent shaking or by shouting in his ear, but relapses at once when left to himself. When the patient is aroused, the respirations become more rapid, and the skin often regains almost at once its normal color. Death very rarely occurs during this second stage of opium-poisoning. When the symptoms do not gradually ameliorate, the third stage, that of prostration, is developed. The coma is now profound, and to arouse the patient may be impossible; the pupils are absolutely contracted, or, as death approaches, are widely dilated; the respirations are distant, slow, feeble, and imperfect, and often interrupted by intervals of death-like quiet; the countenance is at once pallid and cyanosed; the pulse grows more and more rapid and more and more feeble; the skin is cold and moist, finally covered with a clammy sweat. Even yet the patient may recover: if he do so, the return to life is most gradual; if he do not, death occurs generally by failure of the respiration, but amid an almost complete extinguishment of the vital functions.

Although the symptoms which have been narrated are those usually produced by opium, yet in certain individuals the drug provokes quite different phenomena. One of the most common of these departures from the ordinary course of symptoms is an excessive depression following the sleep produced by moderate doses of the medicine. This state is seen, so far as my experience goes, most usually in females of weak, nervous organization, such as are peculiarly liable to attacks of neuralgia. The symptoms are a feeling of weakness and prostration, often accompanied by chilliness, dull headache, and giddiness, but especially marked by intense nausea and frequent vomiting. Very frequently the latter does not occur so long as absolute rest in the horizontal position is maintained: indeed, an almost diagnostic sign of this affection may be found in the fact that the stomach is quiet so long as the patient keeps the head upon the pillow, but the distress occurs at once upon rising up. In some cases this condition of depression even replaces the normal second stage, so that opium, instead of inducing quiet sleep, will provoke alarming depression and vomiting, either with or without drowsiness. Thus, cases have been reported in which one-fourth of a grain, or a somewhat greater quantity, of morphia, hypodermically injected, has been followed at once by syncope, with struggling for breath, and apparently imminent or even present death.* A rarer idiosyncrasy exists in those persons who are rendered by opium very delirious, it may be even wildly so. In certain cases of opium-poisoning, partial or complete convulsions have occurred amidst the more usual phenomena. (Cases, *Brit. Med. Journ.*, 1876, ii., p. 496; *Pacific Med. and Surg. Journ.*, July, 1876.) Severe itching of the skin is a common phenomenon when the action of opium is going off, and there are persons in whom such violent erythema is produced even by therapeutic doses as to forbid the use of the drug (case, *Wien. Med. Presse*, xxiv. 568).

Opium at first sight appears to act so differently upon the lower animals than it does upon man, that it seems necessary to discuss this action by itself.

In 1826, Charvet (*Pereira's Materia Medica*, vol. ii. p. 1035, Philadelphia, 1854) found that opium acts upon all classes of animals, inducing in the invertebrata weakness or paralysis of the contractile tissue, with gradual sinking and death; in fishes, a weakened paralytic condition of the muscular system, associated with convulsions; in birds and mammals, paralysis, convulsions, and stupor. These researches have been recently much extended, but in considering them I shall confine myself to the vertebrata.

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* See Report of the Committee on the Hypodermic Method of Injection, *Medico-Chirurgical Transactions*, vol. l.; see also *Medical Times and Gazette*, 1868, cases reported by Mr. Braine and by Mr. Roberts.

When one or two grains of opium are injected under the skin of a frog (Kölliker, *Virchow's Archiv*, Bd. x. p. 248; J. F. H. Albers, *Virchow's Archiv*, Bd. xxvi. p. 229), in from six to ten minutes a condition of excitability is induced, so that the least touch produces violent tetanic convulsions, which, a little later, also occur without obvious cause. After a time, these convulsions gradually give way to a deepening paralysis. The breathing, previously disturbed, becomes more and more shallow and imperfect, and finally is suspended. Morphia acts, apparently, on frogs in the same manner as opium: at least Drs. Richard Gscheidlen (*Untersuchungen aus dem Physiolog. Laboratorium in Würzburg*, Bd. iii. p. 15) and W. Baxt (*Reichert's Archiv für Anatomie*, 1869, p. 128) have found that in large doses it induces the counterpart of the series of phenomena just described. The latter observer noted, however, that when a minute dose (15.25 milligrammes) was employed, immediately following the injection came a brief period of disquietude; one minute afterwards the frog returned to its normal state, in from six to ten minutes suffered a diminution of excitability, and in from twelve to fifteen minutes fell into a stupor which continued from four to ten hours. After awakening, the reflex excitability seemed greater than normal.*

According to Kölliker, the opium-convulsions take place after the cord has been divided below the medulla, or even as low down as the third vertebra. In a single experiment, tetanus did not occur after division of the cord at the fifth vertebra; but the quietness was probably simply due to exhaustion, as the frog had already been poisoned for a length of time and had suffered section of the medulla and of the cord below the medulla. These facts seem to prove that the convulsions are reflex and of spinal origin. The convulsive movements which are present late in the poisoning would appear to be of peripheral origin: at least, in Albers's experiments (*loc. cit.*) they occurred in limbs whose nerves had been previously cut so as to sever all connection with the nerve-centres. Further, both Kölliker and Albers assert that some of the convulsions are epileptiform,—*i.e.*, of cerebral origin. Further, Dr. S. Meihuizen (*Arch. f. Physiolog.*, vii., 1873) states that the convulsions occur at a time when mechanical irritation fails to induce any response. If these experimental results be correct, opium apparently induces in the frog three kinds of convulsions, of which those of reflex origin are probably the chief.

Kölliker, from his investigations, concluded that opium does not act upon the peripheral nerves of frogs; but the recent very elaborate and apparently accurate experiments of R. Gscheidlen (*Untersuchungen aus dem Physiolog. Laboratorium in Würzburg*, zweiter Theil, 1869, p. 1) have shown that morphia in small doses increases the excitability of the motor nerves and afterwards depresses them; after large doses the period of excitation is short, that of depression soon coming on; and after enormous doses diminution of functional activity is at once manifested. Both Gscheidlen and Kölliker agree that neither the contractile power of the muscles nor the excitability of the motor nerves is destroyed by opium or morphia, although Albers (*Virchow's Archiv*, Bd. xxvi.) asserts that both are extinguished. Gscheidlen calls attention to this disagreement, and states that he has verified his own results by frequent experimentation with enormous doses of the alkaloid.

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* Dr. S. Meihuizen affirms (*loc. cit.*) that this increased reflex activity is only towards chemical and not towards mechanical irritation. This is, however, opposed by such a mass of experimental evidence that I think it must be incorrect.

Experiments upon the sensory nerves are always unsatisfactory, but Gscheidlen (*loc. cit.*, p. 17), employing the method of Pflüger, found that morphia locally applied intensifies and protracts the excitability of an afferent nerve in cases of strychnic poisoning.*

As already stated, the opium-convulsions of the frog are chiefly due to an excitation of the reflex centres of the cord. Gscheidlen has confirmed this by direct experiment, and has also proven that in the latter stages, when the motor functions are depressed, the paralysis is largely of spinal origin, the reflex activity of the cord being greatly lessened.

Our knowledge of the action of morphia upon the nervous system of the frog may be summed up as follows:

Morphia in minute, non-toxic doses causes sleep, followed by augmentation of reflex activity; in large, toxic doses it produces violent convulsions, followed by paralysis. The convulsions are chiefly spinal, and due to a heightened spinal activity, but are to some extent probably, also, of cerebral origin, and later in the attack arise from a direct action of the alkaloid upon the muscle or the nerve-endings therein; the paralysis is caused by a depression of the cord and a diminution of the conducting power in the nerves.

Dr. S. Weir Mitchell has shown (*American Journal of the Medical Sciences*, Jan. 1869, and Jan. 1870) that birds, as represented by pigeons, chickens, and ducks, are very insusceptible to the toxic action of opium and its chief derivative, morphia. It appears to be impossible to kill a pigeon by opium given by the mouth, and of morphia from eight to fifteen grains are required to produce a fatal result; but when given hypodermically from two to three grains of the alkaloid suffice. These results have been in great measure confirmed by Dr. B. W. Richardson, and are no doubt accurate. The symptoms induced have been very uniform: they are unsteadiness, labored breathing, increasing signs of apnœa, *unaltered* pupils, and, finally, general convulsions and death. No true hypnotic effect has been observed, but a curious and very great rise of temperature just before death was noted in one case. As Flourens affirms that a single grain of the aqueous extract of opium will throw a sparrow into a profound stupor, it can scarcely be allowed as proven that the drug acts upon all birds as upon those experimented with by Dr. Mitchell.

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* Perhaps it is appropriate here to call attention to a paper by Dietl and Vintschgau (*Pflüger's Arch.*, Bd. 16), in which it is attempted to be experimentally shown that morphia increases, caffein lessens, and alcohol first lessens and then increases the time required by the nervous system for the recognition of a peripheral irritation.

Upon dogs morphia acts very much as upon man.* In very many cases, if not in the majority, eight to ten grains of the alkaloid injected into a dog of moderate size will cause deep sleep, amounting to coma, so that the animal will remain in any position in which he may be placed. The length and depth of this sleep are, of course, proportionate to the dose: when at all profound, it is accompanied by marked insensibility to pinching and other forms of external irritation. A repetition of irritation, and especially a sudden loud noise or shaking, will, however, arouse the animal, precisely as in man. Indeed, sometimes the dog, even when comatose, seems more than normally sensitive to sudden noise, trembling and starting in an almost convulsive manner. After awaking, the dog shows unmistakable signs of nervous and psychical depression. In walking, the hind legs are dragged, as though semi-paralyzed; the eyes are haggard; the naturally brave animal cowers in a corner or seeks to hide himself, no longer recognizing his master, and does not return to his natural condition for many hours. After smaller doses the effects are proportionately less intense. It has been shown by Harley that in some dogs, precisely as in some people, morphia fails to exert its usual hypnotic action, but produces great depression, as evinced by faintness, prolonged nausea, and retching, interrupted only by intervals of dreamy delirious somnolency.

In the horse (Harley, *loc. cit.*), two or even three grains of morphia hypodermically injected produce sometimes a slight drowsiness, sometimes no perceptible effect. Doses of from four to six grains cause great restlessness and accelerated pulse. The mouth is moist, the temperature of the skin and its secretion increased; the animal paws continually, and treads about in his stall with an almost rhythmical movement. After twelve grains, Harley noticed in some cases very great excitement, as shown by marked increase in the rapidity of the heart's action, by muscular rigidity and tremors, by the animal walking rapidly to and fro, slobbering and sweating profusely. In another horse, after an immediate strong erection of the penis and copious emission of semen, heavy sleep came on, interrupted after the third hour by the usual symptoms of excitement. Thirty-six grains of the acetate caused in a powerful hunter deep comatose sleep, commencing in fifteen minutes and lasting for three hours, when it was replaced by intense restlessness and severe delirium, continuing for seven hours. During this time the animal was perfectly blind.

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* Harley, *The Old Vegetable Neurotics*, p. 107, London, 1869; Claude Bernard, *Archives Générales*, p. 437, vol. ii., 6th series, 1864; J. J. Reese, *American Journal of the Medical Sciences*, Jan. 1871.

Barbier's previous experiments upon the horse (quoted by Prof. Stillé) had yielded results similar to those of Harley. He used larger doses, and found that four drachms of the aqueous extract of opium produced violent tremblings, apparent insensibility to external irritants, convulsions without coma, and death. One hundred grains of the acetate of morphia killed a horse by convulsions in three hours.

In the mouse, according to the experiments of Harley, the first effect of an injection of from one-twentieth to one-twelfth of a grain of morphia is a tonic cramp-like contraction of the muscles, especially of the trunk, of such character that periods of forced rest alternate with a slow, laborious creep, which seems to originate not in the limbs but in the trunk itself. There is in this state no tendency to somnolency, but, on the contrary, an abnormal sensitiveness to loud sounds, which cause the mouse to resume for a moment active running movements. The breathing is irregular, the pulse accelerated, and finally stupor develops itself, and coma deepens into death by apnœa; or, otherwise, recovery, preceded by convulsive movements of the hinder part of the body, is gradually brought about.

In reviewing the action of morphia upon the lower animals, it becomes very evident that whilst we are not in a position to explain all of the symptoms, yet two classes of phenomena are everywhere discernible,—*i.e.*, the spinal and the cerebral,—and that the higher in the scale of life any given animal may be, the more marked are the brain-symptoms. These cerebral phenomena are mostly sleep and stupor; but, as is well known, in some human individuals morphia acts as a delirifacient; and it seems very probable that the peculiar restlessness of the horse under the influence of the alkaloid is due to delirium, and not to spinal excitement.

When looked at in this manner, it seems to me that morphia does not act so differently as is generally believed upon the lower animals and upon man. The immensely higher cerebral organization of the latter, with the immensely greater sensitiveness which it involves, makes the man correspondingly more susceptible to the cerebral action of the drug: hence not only is he affected by much smaller doses of the alkaloid than are the lower animals, but as the spinal symptoms are triumphant in the frog because its spinal system is vastly more developed than its cerebral, so in man the cerebral symptoms mask the spinal because in him the brain is more developed than the cord. The two creatures—man and the frog—occupy the two extremes of the series; between them is probably to be found every gradation.*

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* A curious corroboration of the views expressed in the paragraph is found in the following sentence taken from Althaus (*Diseases of the Nervous System*, New York, 1878, p. 135): "In infants, however, and also in the lower races of mankind, as in negroes and Malays, convulsions are observed after its [opium] ingestion."

The action of opium upon dogs and rabbits is sufficiently close to that upon man to enable us to reason from experiments upon the former as to the influence of the alkaloid upon the circulation and respiration in the latter. Indeed, so far as these functions are concerned, morphia appears to act identically in both instances.

Action on Circulation.—In man, the circulatory phenomena are a slight primary evanescent acceleration of the pulse-rate (see Nothnagel, *Handbuch der Arzneimittellehre*, Berlin, 1870, p. 8), succeeded by slowing and increased fulness and force of the pulse, which is followed by a return to the normal pulse, or a great increase of rapidity and loss of strength during the third stage. R. Gscheidlen has found in rabbits and dogs after the injection of morphia, first an increase in the pulse-rate, then a decrease, and finally return to the normal pulse, or else increased rapidity. Sphygmographic studies of the effects of small doses of morphia have been made with various results by several observers; undoubtedly, in some individuals, therapeutic amounts of the alkaloid depress sensibly the circulation, but in agreement with Riegel and Priesendorffer, it can scarcely be doubted that therapeutic doses have no sensible effect upon the circulation in the ordinary man (see *Deutsches Archiv*, Bd. xxv. p. 48).

The slow, full pulse of the second stage of opium-poisoning is due to an action of the drug upon the inhibitory cardiac nerves, as may also possibly be in some manner the increased arterial pressure; for Gscheidlen (*loc. cit.*, p. 45) has experimentally demonstrated that after section of the vagi morphia is powerless to lower the pulse, and also that division of the nerves during the second stage of morphia-poisoning is followed by an extraordinary rise in the pulse-rate. That the peripheral ends of the vagi are stimulated was proven by the fact that cardiac arrest took place when the distal ends of the cut nerve were more feebly irritated than would suffice to affect the unpoisoned animal; that also the inhibitory cerebral centres are stimulated was demonstrated by the instantaneous very great fall of the pulse-rate, amounting in some cases to one-half in less than half a minute, which ensued upon the injection of a large dose of the alkaloid into the carotid,—*i.e.*, into the brain and the inhibitory centres. The rapid, feeble pulse of the third stage of opium-poisoning Gscheidlen found to be due, at least in a measure, to paralysis of the peripheral vagi; for at such time stimulation of the peripheral end of the cut nerve was powerless to affect the heart.

The experiments of Gscheidlen also indicate that morphia exerts first a *stimulating, then a depressing influence upon the heart-muscle or ganglia*, since, after isolation of the viscus by section of the cord, sympathetic, and pneumogastrics, life being sustained by artificial respiration, a large dose of morphia induced a momentary increase in the number of the cardiac contractions, followed by a marked decrease, and finally extinguishment of the same. This conclusion is confirmed by the experiments of Drs. Sidney Ringer and H. Sainsbury (*British Med.*, March, 1883), who found that opium first increased the power of the cut-out heart of the frog, then depressed it, and finally caused diastolic arrest.

The question of the action of morphia upon the vaso-motor system is of great interest, but cannot at present be fully answered. Gscheidlen believes that it first stimulates and then depresses it, and asserts that after the injection of a large dose the arterioles in the mesentery can be seen to contract, and later (third stage) to dilate. The objections to this sort of evidence are sufficiently stated elsewhere in this book; and the rise of arterial pressure, which he also adduces as an argument, may be accounted for without calling upon the aid of the vaso-motor nerves. While, therefore, it is probable that morphia does exert the influence he claims for it, the question must be still considered as *sub judice:* that the vaso-motor system is not paralyzed even *in extremis*, is shown by Gscheidlen's experiment (*loc. cit.*, p. 52), in which electrical stimulation of the cord at such time induced immediate rise of the arterial pressure. The action of morphia upon the brain is certainly independent of any action on the vessels.*

Action on Respiration.—Death occurs from opium, in the great majority of cases, by failure of the respiration; and that such failure is due to a direct action of the poison upon the respiratory centres in the medulla, is proven by the fact that morphia affects the breathing of dogs and rabbits whose pneumogastrics have been cut, as much as it does those whose nerves are entire (Gscheidlen, *loc. cit.*, p. 64).

Action on Pupil.—Since morphia locally applied does not affect the pupil, it follows that its constitutional action upon the latter is through the nerve-centres. It is probable, but has not, that I am aware of, been experimentally proven, that the contraction of the pupil is due to a stimulation of the oculo-motor nerve-centres, and that the dilatation of the pupil, as death approaches, is due to a paralysis of the same. Indeed, it cannot well be otherwise; for if the primary contraction were due to paralysis of the sympathetic, the secondary wide dilatation would be impossible; the dilating force—*i.e.*, the sympathetic—having been withdrawn, the pupil would not widely expand even if the contracting force—*i.e.*, the oculo-motor—were paralyzed.

In birds (Dr. S. Weir Mitchell, *loc. cit.*) the pupil is not affected; in horses it is widely dilated (Dr. Harley, *loc. cit.*); and in dogs it dilates before contracting (Dr. Reese, *loc. cit.*, apparently confirmed by Experiment number eight, Harley, *loc. cit.*, p. 109), or sometimes remains unchanged (Harley, *loc. cit.*, p. 111). At present these anomalies cannot be explained.

Elimination Action on Kidneys and Intestines.—The exact fate of morphia in the system is uncertain. Various chemists have failed to find it in the urine of persons or animals poisoned by it, but it seems to me established that it is at least in part eliminated with that secretion, as it has been detected by Dr. Hilger (Gscheidlen, *loc. cit.*, p. 32), Bouchardat

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* Consult Binz, *Arch. Exper. Pathol. und Pharm.*, vi., p. 310; Vulpian, *Leçons sur l'Appar. Vaso-Moteur*, ii., p. 156.

(*Schmidt's Jahrbücher*, Bd. cxx.), Lefort (*Journ. de Chimie*, Bd. xi.), and Kausmann (*Beiträge, etc.*, *Inaug. Dissert.*, Dorpat, 1868). Although Prof. Wormley (*Micro-Chemistry*, 503) states that the tests relied upon by Bouchardat are not decisive, it is probable that the conclusions reached in the elaborate research of W. Eliasson are correct (*Beiträge z. Lehre des Schicksals Morphins*, *Inaug. Dissert.*, Königsberg, 1882). They are, that when large amounts are ingested morphine appears freely in the urine, but that after small doses it cannot be found, although a substance is present giving some of the reactions of morphia, from which it is a derivative. The theory that morphia is burnt up in the blood has been advocated by those who have failed to find it in the urine (see E. Landsberg, *Pflüger's Archiv*, 1880, 413), and there is reason for believing that it and other alkaloids are to some extent destroyed in the liver. The amount of the urinary secretion is said to be sometimes increased by morphia; but more generally it is diminished. Retention, which after a full dose of opium is not rare, depends upon the blunting of the sensibility of the bladder. In a series of examinations S. Fubini found that morphine, codeine, narceine, narcotine, and thebaine each increase the excretion of urea in man: upon the lower animals their action seemed to vary greatly (*Hoffmann und Schwalbe Jahresber.*, 1883, 219). It is stated that in habitual opium-eaters morphine occurs in the urine not longer than seven days after the cessation of the habit (*Lond. Med. Record*, 1877, p. 92).

Peristaltic movements, according to the experiments of Prof. Nothnagel (*Archiv f. Path. Anat.*, lxxxix. p. 2), confirmed by J. Ott (*N. Y. Med. Journ.*, 1883), are diminished by small doses of morphine, but increased by toxic doses. The first effect is evidently due to stimulation of the inhibitory nervous apparatus, and the second to paralysis of the same: it is probable that it is the centre which is affected. The experiment which Prof. Nothnagel brings forward as evincing a peripheral action is certainly not pertinent.

Upon the digestive tract opium exerts a very marked influence, checking secretion and causing constipation, acting in these respects more efficiently than does morphia.

THERAPEUTICS.—The chief indications for the use of opium are considered below, *seriatim*. Nearly all of them flow evidently from the known physiological action of the drug; others, however, although established by clinical experience, and undeniable, are not so plain in their philosophy.

1. *To relieve pain.* As an analgesic, opium is without a rival in the materia medica, except it be the anæsthetics. It is used to allay pain arising from any cause whatever, except acute inflammation of the brain, and is preferred to the anæsthetics whenever the pain has any permanency. In *painful spasm* it is especially useful, as it seems very frequently to quiet the motor as well as the sensory disturbance.

2. *To produce sleep.* Sleeplessness occurring in acute disease, and not

dependent upon cerebral inflammation, may very frequently be relieved by opium. While it is often necessary to use the drug freely in such affections as *delirium tremens*, care should be exercised not to overwhelm the nerve-centres by enormous doses. In habitual sleeplessness great caution must be used in the employment of opium, not so much on account of the disturbance of digestion which it is liable to cause, as for fear of producing the "opium habit." Chloral is perhaps a more generally applicable hypnotic than opium. Be this, however, as it may, I have found the combination of morphia and chloral singularly efficient. In low fevers, adynamic delirium often coexists with sleeplessness, and is then best met by opium.

3. *To allay irritation.* In various forms of nervous erethism, opium is most valuable; but when the affection is at all chronic, the dangers of the opium habit should not be lost sight of. On the other hand, in acute cases, as in the excitement which so frequently attends *hæmoptysis*, the drug should be used freely. In many cases of disease, opium is serviceable by sustaining the system against an irritation for the time being irremediable, by blunting the sensibilities. In this way it is useful in the advanced stages of *smallpox*, and in various surgical affections, in which it also does good by allaying pain. In various local irritations, opium is continually employed, as in the *colic* caused by undigested food; in *bronchitis*, it is thus used to quiet cough.

By allaying irritation and pain, opium affords relief in most cases of inflammation; but in certain varieties of the affection it seems to do much more than this, exerting, in some way at present difficult to explain, a life-saving influence. In *peritonitis*, after due depletion, or in cases not requiring depletion, it should always be exhibited in large doses at regular intervals, in such a way as to keep the patient in a state of decided narcotism.

In severe *acute vomiting*, opium is one of the most reliable remedies. It is best used in the form of suppositories. Although, by checking secretion and peristalsis, opium usually causes constipation, yet when *obstruction* of the *bowels* is produced by spasm due to an irritation or inflammation, by relieving the latter the drug will sometimes act as a most efficient laxative.

4. *To check excessive secretion.* For this purpose opium is very largely employed in *diarrhœas*, and is very efficient either alone or in combination with various remedies. In *enteritis* and in *dysentery*, although no less frequently used than in diarrhœa, it is of service rather as an antiphlogistic and analgesic than by checking secretion. In *diabetes insipidus*, the combination of it and gallic acid is, I think, the most generally successful remedy.

In true saccharine *diabetes*, opium is of very great value in many cases, often ameliorating the symptoms, and, in conjunction with restricted diet, sometimes even effecting a cure. Of course, however, like all other known remedies in this disease, it most frequently acts simply as a palliative. According to Dr. Pavey (*Medical Times and Gazette*, June, 1869, p. 641), it affects the quantity of the urine before diminishing the sugar in it.

In severe *mercurial ptyalism*, opium often seems to check the discharge, but certainly is not nearly so powerful in this regard as atropia.

5. *To support the system.* Opium appears in low fevers, and in various protracted adynamic illnesses, to afford actual support to the system in some way not as yet made out. This is especially the case when, from any reason, sufficient food to keep up life cannot be taken or retained.

6. *As a sudorific.* Dr. A. Loomis (*New York Med. Record*, 1873) praises very highly the use of hypodermic injections of morphia in *acute uræmia.* He states that the drug must be given in sufficient quantity to control the convulsions, which it does most happily, at the same time producing profuse diuresis. Dr. Morrison Fiset (*New York Med. Record*, July, 1874) and Dr. Dain (*American Med. Journal*, July, 1874) confirm this. In some instances the remedy has seemed to act very happily, but in one or two cases at the Philadelphia Hospital its exhibition was shortly followed by death in coma. In the form of Dover's powder, opium is very largely used when it is desired to produce sweating, as in the early stages of a "general cold," or other forms of *muscular rheumatism.* With its use should generally be conjoined such measures as "soaking the feet," covering warm in bed, and the free drinking of hot lemonade or hot teas.

TOXICOLOGY.—Sufficient has already been said concerning the course and symptoms of poisoning by opium in ordinary cases.* Sometimes in adults trismus and other convulsive manifestations are added to, or in a measure replace, the usual phenomena, and in children the drug appears at times to overpower the nerve-centres at once, so that the second stage is very much shortened or aborted, and symptoms of collapse, with unconsciousness, are developed very rapidly. The positive diagnosis of opium-poisoning from the symptoms alone is often impossible.† In some cases of congestion of the brain, or of apoplexy, or of uræmia, the phenomena are identical with those sometimes seen in opium-poisoning. I have thought that inequality of the pupils is proof that a case is not one of narcotism; but Prof. Taylor has recorded an instance of opium-poisoning in which it occurred (*Manual of Medical Jurisprudence*, 7th Am. ed., 1873, p. 205).

The indications in the treatment of poisoning by opium are: first, to evacuate the stomach; second, to maintain respiration; third, to keep up the circulation when failing. The first indication may be met in two different ways: by an emetic, and by the stomach-pump or tube used as a siphon. There is often in narcotic poisoning great difficulty in getting an emetic to act, owing to the obtunding of the sensibility of the nervous system by the drug. For this and other reasons, so palpable as not to need mentioning, a prompt stimulant emetic should be used; antimony, on account of its depressing influence, should always be avoided. *Mustard flour* is almost always to be had at once, and is very efficient. A heaped tablespoonful stirred up in a tumblerful of warm water should be exhibited as soon as possible, and, if it fail to act in fifteen minutes, should be repeated; then a powder of thirty grains each of sulphate of zinc and ipecacuanha may be given, to be repeated once or twice, at intervals of fifteen or twenty minutes. Large draughts of warm water should be administered in the intervals, and also between the acts of vomiting, so as thoroughly to wash out the stomach. The stomach-pump* is of no value when the solid drug has been ingested, but, if at hand, is preferable to emetics when a fluid preparation has been taken, because of the promptness of its results.

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* For discussion of effect on nursling and fœtus when morphia is given to mother, see *Amer. Journ. Obst.*, 1877.

† See *Philadelphia Med. Times*, vol. iii., 593; also Dr. Wilks, *Med. Times and Gaz.*, 1863.

To maintain respiration is the ultimate object of all the measures which are commonly undertaken for the purpose of arousing the system in opium-poisoning. Unconsciousness in itself is of no moment, but as it deepens the sensibility of the respiratory centres grows less, and consequently the involuntary breathing is less rapidly or less perfectly performed. More than this, when at all awake, a patient suffering from opium-poisoning can be made to supplement the almost suspended automatic breathing by voluntary respiration; and every effort to induce him to do this should be used. It is often surprising how an apparently unconscious man can be made to breathe by a command shouted in his ear. To keep a patient awake, walking, flagellations with small, *fine* twigs, shaking, shouting, and various other methods which may suggest themselves, should be practiced. Care should always be exercised not to carry these useful measures unnecessarily far, and perhaps add physical exhaustion to the natural prostration of the third stage. I desire also to call especial attention to strong faradaic currents as a means of causing pain, and therefore of rousing the patient, without leaving the bruises and soreness which often result from the severe flagellations practiced.

The cold douche affords an excellent method of rousing the patient and at the same time of especially stimulating respiration. The simplest method of application is to support the head and shoulders of a patient stripped to the waist over a common wash-tub, and to dash the water over the chest and head. The effect is much greater if ice-cold water and water a little hotter than the hand will bear (115° F.) be used in quick succession. In the way of drugs, there are only three substances worthy of mention. Very strong infusions of coffee or of green tea have been long used in opium-poisoning, and recent scientific studies (*British Med. Journ.*, 1874, ii. 698, 699) have shown that in animals doses of morphia otherwise lethal may be successfully combated by thein or caffein; atropia, as a respiratory stimulant, is of the greatest value in opium-poisoning when there is evident failure of respiration

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* The *siphon stomach-pump* may be extemporized by any one. It consists simply of an India-rubber tube three and a half to four and a half feet in length, of proper calibre, which is passed into the stomach. The external end being elevated, water is poured into it until the stomach is full; then, without the tube being allowed to empty itself, the external end is dropped, when, of course, the flow of water is reversed.

(for discussion of its use, see the article on Atropia); and alcohol is to be employed in the stage of depression to sustain the arterial system.*

Whenever life is in evident danger from the insufficiency of natural respiration, the use of artificial respiration should not be postponed, but should be practised to supplement nature, and should be maintained so long as there is any hope. Life has undoubtedly been saved in this way. A case is reported (*N. Y. Med. Journ.*, June, 1880) in which a baby, who had taken one-third grain of morphia, was rescued by artificial respiration kept up, off and on, for twenty-four hours. In some cases excess of bronchial mucus seems to be of serious import. Under such circumstances good might be achieved by placing the patient in an inverted position (*Brit. Med. Journ.*, 1871, ii. 374).

Opium-poisoning usually has no sequelæ; but a case in which *amaurosis* was produced is reported in *Schmidt's Jahrbücher*, Bd. clvii. p. 74, and *glycosuria* is said to have followed the poisoning (*La France Méd.*, 1883, ii.).

In regard to the amount of opium which will cause death, the smallest fatal dose on record is a sixth of a grain of morphia in the adult (Dr. Buskirk, *Washington Post*, Jan. 30, 1878).† According to Dr. A. Calkins (*Quart. Journ. Psychol. Med.*, 1868, vol. ii., 739), four grains‡ of crude opium placed in the ear have caused death; also four grains by the mouth in more than one case. According to the authority just quoted, out of twenty-nine reported cases in which a fluidounce of laudanum was taken, nine died. The maximum doses from which recovery has occurred without emesis are fifty-five grains of the solid opium and six ounces of laudanum. In a babe a day old, one minim of laudanum (E. Smith, *Lancet*, 1854), and in one aged nine months, a few drops of paregoric (Wood, *Bost. Med. Surg. Journ.*, 1858), have proved fatal. Death of an adult female has been attributed, with doubtful accuracy, to thirty grains of Dover's powder, given in divided doses (*Chicago Med. Journ. and Exam.*, July, 1882), and still more hypothetically to a quarter of a grain of morphia (*Boston Med. Surg. Journ.*, Jan. 3, 1885). Recovery is asserted to have occurred after the ingestion of eighteen grains of morphia without vomiting (Dr. Wm. C. Chaffee, *Med. Surg. Rep.*, 1882, xlvii. 697).

ADMINISTRATION.—Whenever it is desired to produce very decided narcotism by the use of repeated doses of opium, the drug should *always be given in liquid form*, since opium pills sometimes become very hard and undergo solution so slowly that they may accumulate in the alimentary canal. On the other hand, in diarrhœas, or in sickness of the stomach, old opium pills are thought by some to act better than more soluble forms of the drug.

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* Various drugs have been stated to be antagonistic to opium and cases of recovery reported. VERATRUM VIRIDE, *Cincinnati Lancet and Clinic*, 1879, iii. 458; *St. Louis Med. and Surg. Journ.*, 1879, xxxvii. 601. ACONITE, *New York Med. Record*, 1880, viii.

† A number of cases are now on record in which death has been produced in the adult by the hypodermic use of from one-sixth to one-half grain of morphia. Consult *Medico-Chir. Trans.*, vol. l.; *Chicago Med. Examiner*, May, 1878; *Quar. Journ. Psycholog. Med.*, 1868, vol. ii. p. 739.

‡ Taken from *Journal de Chimie*, 1831. Assuredly there is a mistake in this case.

Many persons cannot take opium on account of the very great secondary nausea and depression which it produces. It has been supposed that these disagreeable after-effects are due to the narcotina in opium; but this can hardly be, seeing that they often follow the use of the pure alkaloid, morphia. The deodorized tincture of opium agrees with some individuals better than any other preparation of the drug; and, as first pointed out by Dr. Da Costa, by giving a drachm of the bromide of potassium with twenty-five drops of it, the after-effects of the narcotic are often entirely avoided. In many neuralgic women the knowledge of this fact is an inestimable boon; in others the unpleasant symptoms are not averted by the bromide.

Children always bear opium very badly, and to them only the weaker liquid preparations should be given. Dover's powder should especially be avoided. It is probable that in its manufacture on the large scale the ingredients are sometimes not thoroughly mixed: at least I have seen cases in which the symptoms caused by it were seemingly so out of proportion to the dose as to suggest that more than the officinal amount of opium was present.

In *acute vomiting* from any cause, in *dysentery*, in *strangury*, and other irritations of the urino-genital organs, great advantage is often to be gained from the use of opium by the rectum. Suppositories made out of the extract (gr. ss to i), or enemata of laudanum (gtt. xxx to xl), may be used in these cases. The latter should be made by adding the narcotic to a tablespoonful of starch-water.

The dose of opium for an adult is from one to two grains; for a child a year old, one-twenty-fourth of a grain. The U. S. Pharmacopœia directs that opium in its normal moist condition should contain not less than nine per cent. of morphine, and that dried *powdered opium* (*Opii Pulvis*, U. S.), out of which the preparations are made, should contain from twelve to sixteen per cent. of the alkaloid.

The solid officinal preparations of opium are—the *denarcotized opium* (*Opium Denarcotisatum*, U. S.), opium deprived by the action of ether of its narcotina, dose, one to two grains; *pills of opium* (*Pilulæ Opii*, U. S.), containing one grain each; watery *extract* (*Extractum Opii*, U. S.), twice the strength of opium.

Paregoric (*Tinctura Opii Camphorata*, U. S.) has in every fluidounce two grains of opium, besides benzoic acid, oil of anise, and camphor, and, in consequence of the last ingredient, is more constipating than the other preparations of opium, and hence is preferred in diarrhœa-mixtures. It is also much used in cough-mixtures. Dose, fʒi to f℥i. The other liquid preparations all *now* represent ten per cent. of *powdered opium* by weight, and may be given in doses of ten to fifteen minims. The *deodorized tincture* (*Tinctura Opii Deodorata*, U. S.) contains no narcotina, and none of the odorous principle of opium. It therefore is less apt to cause nausea than are the other preparations. Its drop almost equals the minim in size. The other preparations are—*Tinctura Opii*, U. S., or *Laudanum* (one hundred drops to the fluidrachm); *Tinctura Opii Acetata*, U. S., or *Acetated Tincture* (formerly gr. xlviii to f℥i); *Vinum Opii*, U. S., or *Sydenham's Laudanum* (formerly ℥i to f℥i); *Acetum Opii*, U. S., or *Black Drop* (formerly gr. lxxv to f℥i).

MORPHINA.* U.S.

This alkaloid occurs in minute, colorless, shining crystals, according to Guy melting at 330° F. and subliming at 340° F.; insoluble in cold and almost so in boiling water; only slightly soluble in cold alcohol and ether; freely soluble in boiling alcohol and in the fixed and volatile oils.

The following are some of the most sensitive and characteristic tests. In a solution of the alkaloid in concentrated sulphuric acid, which has been allowed to stand from ten to twelve hours, or has been heated for half an hour to 100° C. or momentarily to 150° C. and allowed to cool, the faint-reddish violet changes at the point of contact to a deep-blue violet upon the addition of dilute nitric acid or of a crystal of saltpetre. Morphia with concentrated sulphuric acid makes a colorless solution, which on strong heating becomes red, violet, dirty green. With concentrated nitric acid it makes a red color, and finally a yellowish solution. With the neutral chloride of iron morphia strikes a blue color, perceptible only when the test contains one part of the alkaloid in six hundred. Less characteristic, but much more sensitive, is the iodine test, with which, according to Husemann, one-ten-thousandth part of morphia can be recognized. Iodic acid, in the form of a mixture of iodate of potassium and sulphuric acid, is to be added to the suspected solution. If morphia be present, iodine will be set free, and can be recognized by the starch test.

The *Acetate* (MORPHINÆ ACETAS), *Sulphate* (MORPHINÆ SULPHAS), and *Hydrochlorate* or *Muriate of Morphine* (MORPHINÆ HYDROCHLORAS) are all officinal. The first is a white powder; the last two occur snow-white in feathery crystals. They are all soluble in water, and are of a bitter taste.

THERAPEUTICS.—The salts of morphia differ in their therapeutic value / from opium chiefly in that they act with less power as sudorifics and in checking secretion in the bowels, and consequently constipating. The smallness of their dose and their perfect solubility fit them for hypodermic use. Almost the only purpose for which they are used in this way is to relieve pain. The advantages of the method are the quickness of the results and

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* For spectrum analysis of morphia, see *New York Medical Journal*, 1874.

Morphine
1. Weaker sudorific
2. [illegible] likely to constipate
3. Rapid action

the increased power of relieving suffering which the remedy seems to acquire. In cases of severe pain, hypodermics are invaluable; but it must be borne in mind that sometimes they cause most unpleasant symptoms. I have seen very alarming results from the injection of one-sixth of a grain, and half a grain has produced death. In females, unless very robust, the maximum dose should be one-eighth of a grain; in men, one-sixth to one-quarter. The dose of a salt of morphia corresponding to a grain of opium is one-quarter of a grain. The dose of the formerly officinal solution (*Liquor Morphiæ Sulphatis*, U. S. 1870,—gr. i to f℥i) is one to three drachms. *Magendie's Solution of Morphia* contains sixteen grains to the fluidounce: it is not officinal, and should not be kept in the apothecaries' shops. The *Suppositories* (*Suppositoria Morphiæ*, U. S.) contain each half a grain of morphia.

NARCEIN.

This alkaloid, which is not officinal, was discovered by Pelletier in 1832. "It crystallizes out of its watery, alcoholic, and dilute acid solutions in long, white, four-sided, rhombic prisms, or in bunched masses of fine acicular crystals, odorless, and of a taste at first bitterish, but later styptic." (Pelletier, Hesse, Winckler—Husemann, *Die Pflanzenstoffe.*) According to Pelletier, it is soluble in 375 parts of water at 13° C.; according to Hesse, in 1285 parts at 12° C.; whilst Dr. S. Weir Mitchell found that a specimen prepared by Merck dissolved in 1000 parts, one prepared by Powers & Weightman in 4000 parts, and one of unknown European manufacture in 2100 parts, of distilled water at 60° F. Its saturated solution in boiling water on cooling fills with crystals. Concentrated nitric acid dissolves narcein with a yellow color, and the solution on being heated gives off reddish fumes; iodine makes with it a bluish-black mass, which forms a colorless solution in boiling water, but on cooling separates; with concentrated sulphuric acid narcein strikes a brown color, and finally makes a clear yellow solution (Husemann).

PHYSIOLOGICAL ACTION.—According to Baxt (*Reichert's Archiv*, 1869, p. 126), three or four centigrammes (0.46 to 0.62 gr.) of narcein, when injected into a frog, produce, in from ten to fifteen minutes, a semi-comatose condition, in which the batrachian makes no resistance or effort when laid upon his back or in other unnatural position. The respiration and circulation are not disturbed. The frog can be aroused by strong irritation, and when awake seems perfectly conscious. In three to six hours he comes out of his lethargic condition apparently unaffected. Albers (*Virchow's Archiv*. vol. xxvi.) found that one grain produces in the frog sleep, reflex and spontaneous convulsions, and, after seventy-four hours, death. According to Ott, the convulsions are chiefly spinal, the muscles also being affected. Dr. S. Weir Mitchell (*Amer. Journ. Med. Sci.*, Jan. 1870) found nine grains of the alkaloid to have very little effect upon pigeons, causing only abnormal quietness. In Baxt's experiments upon rabbits and guinea-pigs, fifteen centigrammes (2.3

gr.) had no perceptible influence; and on dogs Dr. S. Kersch (*Schmidt's Jahrbücher*, Bd. cxli. p. 15), and also Dr. Harley (*The Old Vegetable Neurotics*, p. 143), found moderate doses (26 ctgr. Kersch) equally inert. In a mouse (Harley) one-half grain caused tranquil sleep, with, after a time, tremors, from which the animal recovered, to be taken suddenly, some hours later, with fatal convulsions. At the post-mortem the tubules of the kidneys were found completely choked up with the alkaloid, which had crystallized in them and produced a mechanical suppression of urine, to which death was probably due. Schroff (quoted by Rabuteau), Fronmüller (*Schmidt's Jahrbücher*, Bd. cxli. p. 15), Harley, Mitchell, and Da Costa (*Pennsylvania Hospital Reports*, 1868), have found narcein to act very feebly upon man. Harley gave one grain hypodermically, Da Costa two and one-half grains by the mouth, and Mitchell took five grains himself, with the result of only causing some headache; and Fronmüller has exhibited as much as twenty grains with equally negative results.

These investigations are in close concord, and seemingly conclusive; and the study of Dr. Da Costa upon man was very full and exhaustive. They are opposed by a number of seemingly equally conclusive investigations made by various French and German observers. Much of the interest that has been manifested in the alkaloid arose from the assertion of Claude Bernard in 1864 (*Archives Générales*, 6e sér., t. iv. p. 459), that it is the most pleasant and certain hypnotic of any of the opium alkaloids. He experimented upon dogs, guinea-pigs, rats, pigeons, sparrows, and frogs, and in all of them there was produced deep sleep, closely resembling natural sleep, with benumbed but not destroyed sensibility. The irritability of the morphia-sleep was wanting, and no secondary depression followed. Seven to eight centigrammes (1.65 gr.) was sufficient to throw a dog into the profoundest slumber. As early as 1852, Lecomte (Husemann, *Die Pflanzenstoffe*, p. 176) had affirmed that 0.1 grm. (1.53 gr.) of narcein thrown into the jugular vein of a dog would produce deep sleep, and very recently Rabuteau has confirmed the results of Bernard. Further, Behier (*Bulletin Thérap.*, t. lxvii.), Debout (*Ibid.*), A. Eulenburg (*Schmidt's Jahrbücher*, Aug. and Oct. 1866), Liné (*Journal de Pharmacie et de Chimie*, 4e sér., t. iii.), also assert as the result of experience that narcein, in doses of one-half grain to a grain, produces in man pleasant, persistent sleep. Rabuteau (*loc. cit.*) also agrees with this, except in placing the dose somewhat higher,—viz., at from ten to twenty centigrammes (1.53 to 3.06 gr.). Oetinger (*Das Narcein als Arzneimittel*, Diss. Inaug., Tübingen, 1866) also asserts that decidedly larger doses of narcein than of morphia are required to obtain any action.

As seemingly these opposing results are all true, the only possible explanation is that different substances were used by the different sets of observers under the one name. As the greatest care was practiced by Harley and Mitchell in obtaining the alkaloid pure, and as Claude Bernard states expressly that the substance used by him was soluble in twenty parts of water, it is most probable that the former observers really had, and that Bernard did not have, the narcein of Pelletier.

It is, at any rate, a very plain deduction from the above facts that, if it be so difficult—nay, impossible—to obtain in commerce a uniform reliable narcein, it is not proper to use it as a medicine.

CODEINA. U.S.

Albers found that one grain of the muriate of codeine would produce in the frog, twenty minutes after its injection, tetanic cramps, alternating with convulsions: evidently reflex, since the slightest touch would call them forth. After a time the convulsive excitement grew less and less; the fore feet lost their sensitiveness first, but finally a paroxysm could no longer be provoked by touching the hind feet. The pupils at this time were widely dilated. Death occurred by failure of respiration, the heart continuing to beat a quarter of an hour after the extinguishment of all other movements. In Woldemar Baxt's (*Reichert's Archiv*, 1869, p. 125) experiments, three centigrammes (0.45 gr.) produced in the frog deep sleep, lasting three or four hours. On awaking, the frog seemed more sensitive than natural to external irritation. Six centigrammes produced sleep more quickly, and following the deep sleep a stage of excessive sensitiveness, during which external irritation produced repeated cramp-like contractions. M. Wachs (quoted by Husemann, *Die Pflanzenstoffe*, p. 163) observed phenomena similar to those detailed by Albers, but noted a peculiarity of gait in the frog preceding the convulsive stage, owing apparently to disturbance in the innervation of the adductors. Wachs also found that .010 gramme (0.15 gr.) produced in the pigeon only increased rate of respiration and sleepiness, whilst larger fatal doses caused restlessness, inability to stand, movements backward and in a circle, disturbance of respiration with gasping, cramps of single muscles, and finally convulsions, mostly clonic, frequently repeated, and followed by an adynamic condition, terminated by sudden death. In Dr. S. Weir Mitchell's experiments (*Amer. Journ. Med. Sci.*, Jan. 1870, p. 26), seven grains produced violent non-tetanic convulsions, ending fatally in one minute; and one grain caused similar symptoms, terminating fatally in eight minutes. Dr. Ott (*Opium Alkaloids*) found that the convulsions in the frog are spinal, but that the muscles are affected.

According to Husemann (*loc. cit.*, p. 133), Kunkel, in 1833, from his experiments arrived at results similar to the recent ones of Bernard. The latter observer found that five centigrammes (.075 gr.) produced in dogs a sleep similar to, but not so profound as, that of morphia, with less benumbing of sensation, and not followed by any symptoms of depression.

These results have been called in question by Harley, and it seems most probable that Claude Bernard used something more than codeine in his experiments. Certainly Harley found that one to two grains of the alkaloid produced in the dog disturbance of respiration, languor, and convulsive twitchings, but no sleep. Moreover, Husemann states that, after fatal doses, Wachs observed similar symptoms in the dog and in the rabbit, as follows: falling of the head, trembling, spasmodic movements of the eyes and lips, rarely trismus, movements in a circle and backwards, weakness of the legs, with hurried respiration and prominence of the eyeballs as prodromes; later in the poisoning there were severe convulsions, after one or many paroxysms of which great weakness developed, ending in death. Barnay, in experiments upon dogs, cats, and rabbits, found that the convulsions were the most prominent symptom (*De la Codeine*, Paris, 1877). Falck affirms (*Deutsches Klinik*, 1870) that there are two forms of poisoning produced by codeia,—the one tetanic and the other soporific,—corresponding apparently to the different results of various observers.*

As a hypnotic in man, codeia has been used by Magendie, Berthé, Aran, Krebel, Reissner, Robiquet, and others, some of whom assert that the sleep produced by it is followed by nausea or other symptoms of depression, whilst others deny this. It does not seem necessary to discuss in detail the researches of the authorities alluded to, but it may be well to give the results of one or two of these observers more in full.

Robiquet in a series of experiments found that doses of 0.01 to 0.03 gramme (.15 to .46 gr.) produced a feeling of contentment, calmed nervousness, and induced refreshing sleep, whilst 0.1 to 0.2 gramme (1.53 to 3.07 gr.) caused deep sleep, followed by nausea and vomiting; 0.1 gramme (1.53 gr.) caused in children very alarming symptoms. Harley has found in a number of experiments that, given by the mouth, codeia is a very uncertain and feeble hypnotic, four grains producing simply accelerated pulse, contracted pupils, and some giddiness, followed by nausea and vomiting. When the drug is given subcutaneously, "somnolency," he states, "is a more prominent effect, but only occurs in certain individuals." His hypodermic dose is one to two grains. On the other hand, Dnorzak and Heinrich found that codeia in doses of 0.1 gramme caused gastric uneasiness and pain, some salivation, nausea, heat, and feeling of weight in the head, some confusion of thought, very marked reduction of the pulse-rate, and very marked tremors affecting the whole body; and Mitchell took five grains of the alkaloid without inducing other effects than a rise of twenty per minute in the pulse-rate, nausea, slight giddiness, and a sense of heaviness about the head. Dr. A. S. Myrtle records (*British Medical Journal*, 1874, i. 478) a case of severe poisoning by four grains of codeia prepared by the Messrs. Smith of Edinburgh. There was first vascular excitement and exhilaration, then depression with great anxiety, nausea and vomiting, pale, cool, clammy skin, slight contraction of pupil, and sleeplessness, with slight delirium.

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* From what he says on p. 226, it is probable that Falck used two preparations of codeia,—one made in his own laboratory, the other obtained from Merck. It is not possible to determine from his text whether this had anything to do with the different results he obtained.

It is very evident that these various observers have not had the same principle. In my own experience codeia, prepared by Powers & Weightman, has failed to act in grain doses as a hypnotic. There are no reasons for believing that it has any advantages of morphia, whilst its uncertainty is very great. I have found it of some value in one-half grain doses in quieting bronchial irritation.

The remaining active principles of opium being objects of physiological rather than of clinical interest, I shall allude only to their physiological actions.

Narcotina.—Although in Dr. Albers's experiment (*loc. cit.*, p. 244) one grain of narcotina proved fatal to a frog without the production of convulsions, yet the united testimony of Claude Bernard (*loc. cit.*, p. 462), of Baxt (*loc. cit.*, p. 124), of Rabuteau (*loc. cit.*, p. 266), of Mitchell (*loc. cit.*, p. 23), and of Ott (*loc. cit.*), show that in the lower animals this alkaloid produces, when given in sufficiently large dose, active spinal convulsions. In small dose (one-half grain) it causes, according to Albers and to Baxt, in frogs a semi-comatose state. In larger dose (1.2 grains) the last observer found it to induce in the same batrachian very decided convulsions, similar to those of morphia-poisoning. Dr. Mitchell states that from two to three grains produce violent and fatal convulsions in the pigeon. Claude Bernard ranks narcotina above morphia and codeia, next to papaverina, as a convulsant in the lower animals. Yet Orfila found thirty grains necessary to kill a dog, and Baxt has given about two grains to rabbits and to guinea-pigs without producing any symptoms.

Man is no more sensitive to narcotina than the lower animals, if indeed he be so sensitive. Twenty and thirty grains of it have frequently been taken without effect, and doses of one hundred and twenty grains are said to have been exhibited with no greater result.

Thebaia, or *Paramorphia.*—Magendie, Orfila, Albers, Baxt, Claude Bernard, F. W. Müller (*Das Thebaia*, Diss. Inaug., Marburg, 1868), Harley, Fraser, Mitchell, Rabuteau, and other observers, all agree as to the very great similarity between the action of thebaia and that of strychnia. Falck (*Deutsches Klinik*, 1869) divided the general symptoms produced by the poison in mammals into three stages: the prodromal period, in which there was restlessness, combined with a desire to creep into corners, urination, increased frequency of respiration, and some stiffness of the leg; the second stage, in which there were violent strychnic convulsions, greatly interfering with respiration, and sometimes producing cyanosis; the third period, in which there was paralytic muscular weakness, with apparent death, ending, after a time, in real death. The third stage was usually momentary, and seems to me to have been merely the dying, which occurred when the animal was exhausted and cyanosed by the convulsions. A notable symptom of thebaia-poisoning is the increase of bodily temperature, which Falck found to amount to from ½° to 3° C. On pigeons (Falck and Ott) thebaia acts as upon mammals, and in frogs it produces the most violent tetanic spasms The convulsions are undoubtedly spinal, as they occur after section of the cervical cord.

The only detailed study of the physiological action of thebaia yet made is that of J. Ott (*Boston Medical and Surgical Journal*, April, 1875), who found that the alkaloid does not directly affect the motor or sensory nerves or the striated muscles. The same observer also determined that thebaia exerts no influence on the inhibitory cardiac nerves, but does increase the arterial pressure by stimulating the vaso-motor centres, and probably also by stimulating the intra-cardiac ganglia. Thebaia is undoubtedly an exceedingly active poison. According to Albers, less than half a grain will cause violent tetanus in a frog, and in Ott's experiments .011 gr. produced very decided symptoms in the same animal. Harley found two grains sufficient to kill a bitch, and in Falck's experiments a grain and a half injected hypodermically killed a dog in ten minutes. The alkaloid must act upon man as upon the lower animals; yet Fronmüller (*Klinische Studien der Nark. Arzneimittel*, Erlangen, 1869) affirms that he has given it in as high as six-grain doses without producing any symptoms, and that Prof. Leidesdorff (*Wiener Med. Wochenschrift*, No. 34, 1868) had had similar results. Rabuteau is said to have taken 1.5 gr. without decided symptoms. On the other hand, Eulenburg found one four-hundredth of a grain to cause increased respiration, pulse-rate, and temperature, with sometimes wide dilatation of the pupil (quoted by Ott). It seems impossible to avoid the conviction that the drug used by Fronmüller must have been either very impure or else not thebain at all. Husemann (*Arch. Exper. Path. und Therap.*, ix. 422) has found chloral strongly antidotal to toxic doses of thebain.

Papaverina.—A great deal of discrepancy exists among observers as to the physiological action of papaverina, obviously dependent upon variations in the purity of the specimens which they have used. Schroff and Hoffmann believe it to be inert in man, since the latter observer took about seven grains without any effect being induced.

Albers and Claude Bernard claim that on animals it acts as a convulsant resembling thebaia; whilst Baxt asserts that in frogs it produces profound sleep, with great slowing of the heart's beat, but without tetanus, and that it even acts as an antitetanic in the poisoning of codeia and of morphia. He also finds that rabbits and guinea-pigs bear enormous doses of it. Rabuteau says two to three centigrammes produce violent convulsions in the frog, but twenty-five centigrammes in the dog cause no symptoms; yet in Baxt's experiments four to ten centigrammes served to cause profound coma in the latter animal. Ott affirms it is both narcotic and convulsant, and produces a condition of the muscles similar to that caused by veratria. These statements are irreconcilable, and no opinion can be arrived at until new researches, prefaced by a rigid chemical study of the alkaloid used, are entered upon.

Laudania, discovered by Hesse (*Annalen der Chemie und Pharmacie*, viii., Supplement. Bd., p. 272), has been elaborately investigated by Prof. Falck, of Marburg* (*Deutsche Klinik*, 1874, p. 298). He finds that there are three stages of its poisoning: first, hurried respirations, pupils contracted or dilated, muscular twitchings and convulsive tremblings; second, convulsions closely resembling those of strychnia-poisoning; third, adynamia, apparent death, and finally death from failure of respiration, the heart being the last part of the body to die.

Porphyroxia, according to Albers, acts upon the frog as the most powerful of all the convulsant opium alkaloids. Baxt (*loc. cit.*, p. 123) found it in doses of two to three milligrammes (.030 to .045 grain) to throw the frog into a semi-comatose condition, followed in fifteen to twenty minutes by most violent convulsive excitement. In sparrows one milligramme (.015 gr.), and in pigeons a larger dose, produced violent tremors, lasting ten to fifteen minutes, and followed by a state of semi-coma. In guinea-pigs ten to twenty milligrammes (.15 to .30 gr.), and in rabbits a one-fourth to one-third larger dose, caused violent tetanic cramps; larger doses produced speedily fatal convulsions. According to Schroff, 1.5 grains are without influence upon man.

Cryptopia, according to Harley, causes in dogs wild delirium, with dilated pupils, followed by tetanic spasms. In the mouse, small doses produce some delirious excitement, followed by somnolency; while large doses cause heavy sleep, and death from failure of the respiration. In the more detailed investigation of Immanuel Munk (*Wirkung des Cryptopin*, Inaug. Diss., Berlin, 1873) it was found that the convulsions did not occur when artificial respiration was performed, and are, therefore, probably not spinal. The death was preceded by loss of reflex excitability from spinal depression, and was due to respiratory paralysis. Enormous doses also killed the cardiac muscle. A grain and a half injected beneath the skin by Harley caused in some persons intense drowsiness; in others, very slight symptoms. According to Dr. Ott, it is narcotic, exciting and then depressing the motor spinal centres, paralyzing spinal sensory centres, lessening functional activity of the motor nerves, and lowering heart-action by an influence on its muscle.

Meconia, according to Albers (*loc. cit.*, p. 248), produces in (0.045 grm.) the frog mild tremors, lessening of sensation, and finally death. On the higher animals its poisonous action is not very great. Orfila injected 0.06 grm. (0.9 gr.) into the jugular vein of a dog, without effect. Harley gave two grains hypodermically to the same animal, with no further result than a little abnormal quietness. According to the same observers, subcutaneous injections of fourteen grains have no effect on the horse, but one-sixth of a grain produces very decided hypnotism in the mouse. On man, Dublanc

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* The following is the minimum fatal dose of alkaloids for rabbits, per kilogramme (2 lb. 5½ drm.) of weight, as determined by Falck: strychnia, 0.0006 gramme; thebaia, 0.0120 grm.; laudania, .0250 grm.; hydrocotarnia, 0.1600 grm.; morphia, 0.7200 grm.

(*Pharm. Centralblatt*, 1832), Schroff (*Medicin. Jahrb.*, 1870), Fronmüller (*Klinische Studien Narcot. Arzneien*), and Harley have found meconia, when given by the mouth, inert in doses varying from one to eighteen grains. Harley, however, claims that in doses of one to two grains given hypodermically it acts upon man as a very excellent hypnotic; but Fronmüller has injected nearly two grains, with entirely negative results.

Hydrocotarnia.—The physiological action of this alkaloid has been investigated by F. A. Falck (*London Medical Record*, i. 218). He finds it more actively poisonous to rabbits than is morphia. In some of his experiments it produced tetanic convulsions, in others coma and stupor. In frogs the symptoms were always tetanic.

In regard to the action of *Pseudomorphia* and *Opiania* we have little or no knowledge. Sertürner, the discoverer of *Meconic Acid* (quoted by Albers), found it in his experiments to be actively poisonous; but Sömmering and Albers have come to an opposite conclusion. Large doses (one to two grains) do, however, affect frogs, although slowly, inducing a stupor-like condition, with convulsions.

CANNABIS INDICA—INDIAN CANNABIS—INDIAN HEMP. U.S.
CANNABIS AMERICANA—AMERICAN CANNABIS. U.S.

Under the respective names which head this article, the U. S. Pharmacopœia recognizes the dried tops of the Cannabis sativa, or common hemp plant, as it grows in India and in our own country.

EXTRACTUM CANNABIS INDICÆ—EXTRACT OF INDIAN HEMP. U.S.

The alcoholic extract of Indian hemp is a blackish, resinous extract, of a decided narcotic odor and a peculiar taste. In the East, hemp and its educts are used as narcotic stimulants. *Gunjah* is the dried plant as sold in the bazaars of Calcutta for smoking. *Churrus* is the resinous exudation with the epidermis, etc., scraped off the leaves. *Hashish* is an Arabian preparation of the drug. The resin, which represents the activity of hemp, is sometimes known as *Cannabin.* It is best obtained by precipitating the saturated tincture with water containing an alkali. Hemp also contains a trace of volatile oil.

Physiological Action.—When given in full doses, cannabis indica produces a feeling of exhilaration, with a condition of reverie, and a train of mental and nervous phenomena which varies very much according to the temperament or idiosyncrasies of the subject, and very probably also, to some extent, according to the nature of his surroundings. The sensations are generally spoken of as very pleasurable; often beautiful visions float before the eyes, and a sense of ecstasy fills the whole being; sometimes the venereal appetites are greatly excited; sometimes loud laughter, constant giggling, and other indications of mirth are present. Some years since, in experimenting with an extract made from the American plant, I took a very large dose, and described the result as follows (*Proceed. Amer. Philosoph. Soc.*, 1869, vol. xi. p. 226):

"About half-past four P.M., September 23, I took most of the extract. No immediate symptoms were produced. About seven P.M. a professional call was requested, and, forgetting all about the hemp, I went out and saw my patient. Whilst writing the prescription, I became perfectly oblivious to surrounding objects, but went on writing, without any check to or deviation from the ordinary series of mental acts connected with the process, at least that I am aware of. When the recipe was finished, I suddenly recollected where I was, and, looking up, saw my patient sitting quietly before me. The conviction was irresistible that I had sat thus many minutes, perhaps hours, and directly the idea fastened itself that the hemp had commenced to act, and had thrown me into a trance-like state of considerable duration, during which I had been stupidly sitting before my wondering patient. I hastily arose and apologized for remaining so long, but was assured I had only been a very few minutes. About seven and a half P.M. I returned home. I was by this time quite excited, and the feeling of hilarity now rapidly increased. It was not a sensuous feeling, in the ordinary meaning of the term; it was not merely an intellectual excitation; it was a sort of *bien-être*,—the very opposite to *malaise*. It did not come from without; it was not connected with any passion or sense. It was simply a feeling of inner joyousness; the heart seemed buoyant beyond all trouble; the whole system felt as though all sense of fatigue were forever banished; the mind gladly ran riot, free constantly to leap from one idea to another, apparently unbound from its ordinary laws. I was disposed to laugh; to make comic gestures; one very frequently recurrent fancy was to imitate with the arms the motions of a fiddler, and with the lips the tune he was supposed to be playing. There was nothing like wild delirium, nor any hallucinations that I remember. At no time had I any visions, or at least any that I can now call to mind; but a person who was with me at that time states that once I raised my head and exclaimed, 'Oh, the mountains! the mountains!' Whilst I was performing the various antics already alluded to, I knew very well I was acting exceedingly foolishly, but could not control myself. I think it was about eight o'clock when I began to have a feeling of numbness in my limbs, also a sense of general uneasiness and unrest, and a fear lest I had taken an overdose. I now constantly walked about the house; my skin to myself was warm, in fact my whole surface felt flushed; my mouth and throat were very dry; my legs put on a strange, foreign feeling, as though they were not a part of my body. I counted my pulse and found it one hundred and twenty, quite full and strong. A foreboding, an undefined, horrible fear, as of impending death, now commenced to creep over me; in haste I sent for medical aid. The curious sensations in my limbs increased. My legs felt as though they were waxen pillars beneath me. I remember feeling them with my hand and finding them, as I thought at least, very firm, the muscles all in a state of tonic contraction. About eight o'clock I began to have marked 'spells,'—periods when all connection seemed to be severed between the external world and myself. I might be said to have been unconscious during these times, in so far that I was oblivious to all external objects, but on coming out of one, it was not a blank, dreamless void upon which I looked back, a mere empty space, but rather a period of active but aimless life. I do not think there was any connected thought in them; they seemed simply wild reveries, without any binding cord,—each a mere chaos of disjointed ideas. The mind seemed freed from all its ordinary laws of association, so that it passed from idea to idea, as it were, perfectly at random. The duration of these spells to me was very great, although they really lasted but from a few seconds to a minute or two. Indeed, I now entirely lost my power of measuring time. Seconds seemed hours; minutes seemed days; hours seemed infinite. Still I was perfectly conscious during the intermissions between the paroxysms. I would look at my watch, and then after an hour or two, as I thought, would look again and find that scarcely five minutes had elapsed. I would gaze at its face in deep disgust, the minute-hand seemingly motionless, as though graven in the face itself; the laggard second-hand moving slowly, so slowly. It appeared a hopeless task to watch during its whole infinite round of a minute, and always would I give up in despair before the sixty seconds had elapsed. Occasionally, when my mind was most lucid, there was in it a sort of duplex action in regard to the duration of time. I would think to myself, It has been so long since a certain event,—an hour, for example, since the doctor came; and then reason would say, No, it has been only a few minutes; your thoughts or feelings are caused by the hemp. Nevertheless, I was not able to shake off this sense of the almost indefinite prolongation of time, even for a minute. The paroxysms already alluded to were not accompanied with muscular relaxation. About a quarter before nine o'clock, I was standing at the door, anxiously watching for the doctor, and when the spells would come on I would remain standing, leaning slightly, perhaps, against the doorway. After awhile I saw a man approaching, whom I took to be the doctor. The sounds of his steps told me he was walking very rapidly, and he was under a gas-lamp, not more than one-fourth of a square distant, yet he appeared a vast distance away, and a corresponding time approaching. This was the only occasion in which I noticed an exaggeration of distance; in the room it was not perceptible. My extremities now began to grow cold, and I went into the house. I do not remember further, until I was aroused by the doctor shaking or calling me. Then intellection seemed pretty good. I narrated what I had done and suffered, and told the doctor my opinion was that an emetic was indicated, both to remove any of the extract still remaining in my stomach, and also to arouse the nervous system. I further suggested our going into the office, as more suitable than the parlor, where we then were. There was at this time a very marked sense of numbness in my limbs, and what the doctor said was a hard pinch produced no pain. When I attempted to walk up-stairs, my legs seemed as though their lower halves were made of lead. After this there were no new symptoms, only an intensifying of those already mentioned. The periods of unconsciousness became at once longer and more frequent, and during their absence intellection was more imperfect, although when thoroughly roused I thought I reasoned and judged clearly. The oppressive feeling of impending death became more intense. It was horrible. Each paroxysm would seem to have been the longest I had suffered; as I came out of it, a voice seemed constantly saying, 'You are getting worse; your paroxysms are growing longer and deeper; they will overmaster you; you will die.' A sense of personal antagonism between my will-power and myself, as affected by the drug, grew very strong. I felt as though my only chance was to struggle against these paroxysms,—that I must constantly arouse myself by an effort of will; and that effort was made with infinite toil and pain. I felt as if some evil spirit had control of the whole of me except the will-power, and was in determined conflict with that, the last citadel of my being. I have never experienced anything like the fearful sense of almost hopeless anguish and utter weariness which was upon me. Once or twice during a paroxysm I had what might be called night-mare sensations; I felt myself mounting upwards, expanding, dilating, dissolving into the wide confines of space, overwhelmed by a horrible, rending, unutterable despair. Then, with tremendous effort, I seemed to shake this off, and to start up with the shuddering thought, Next time you will not be able to throw this off, and what then? Under the influence of an emetic I vomited freely, without nausea, and without much relief. About midnight, at the suggestion of the doctors, I went up-stairs to bed. My legs and feet seemed so heavy I could scarcely move them, and it was as much as I could do to walk with help. I have no recollection whatever of being undressed, but am told I went immediately to sleep. When I awoke, early in the morning, my mind was at first clear, but in a few minutes the paroxysms, similar to those of the evening, came on again, and recurred at more or less brief intervals until late in the afternoon. All of the day there was marked anæsthesia of the skin. At no time were there any aphrodisiac feelings produced. There was a marked increase of the urinary secretion. There were no after-effects, such as nausea, headache, or constipation of the bowels."

The sense of prolongation of time which I experienced was to me very remarkable, but is not uncommon in these cases. It is evidently due to the immense rapidity of the succession of ideas. The mind, without doubt, measures time by the duration of its own processes, and when an infinitude of ideas arise before it in the time usually occupied by a few, time becomes infinitely prolonged to the mind. It is a lifetime in the minute. A very common mental phenomenon, not yet mentioned, is a condition of double consciousness, a sense of having two existences, of being at the same time oneself and somebody else.

In some cases Indian hemp produces, in addition to or even in the place of the symptom already spoken of, marked disturbances of motility. Convulsions have been noticed by Dr. Lawrie (*Stillé's Therapeutics*, vol. i. p. 772), and local spasms, with salaam convulsions, by Dr. F. H. Brown. According to Dr. O'Shaughnessy, the induction of catalepsy is not rare among the Hindoos.

Whatever may be the symptoms of the first stage, sooner or later, if the dose be sufficient, drowsiness comes on. Generally, before it is marked, partial anæsthesia, often with partial loss of strength, is manifested, especially in the lower limbs. The pupils are dilated, the pulse is quickened, and finally the subject falls into a heavy sleep, out of which he generally awakes hungry, without any of the wretched gastric sensations or the malaise felt after an opiate. Confusion of thought, however, may persist for some hours. Cannabis exerts no constipating influence upon the bowels, and appears to increase, rather than decrease, the excretion of the kidneys.

THERAPEUTICS.—Leaving out of sight the employment of the medicine by alienists, hemp has been used in this country chiefly for the *relief of pain*, but also to some extent as a *hypnotic*. As an analgesic, it is very much inferior to opium, but may be tried when the latter is for any reason contra-indicated. In full doses, in *neuralgic* pains, it certainly often gives relief. It has been very largely employed to induce euthanasia in the advanced stages of *phthisis*, and constitutes, it is said, a popular nostrum employed for that purpose. In *tetanus*, Indian hemp has been used quite largely, and until within a short time was, after opium, one of the few known drugs of service. Dr. Roemer (*St. Louis Medical and Surgical Journal*, p. 363, 1873) has collected thirty-five cases, with twenty-one recoveries and fourteen deaths.

ADMINISTRATION.—The action of the preparations of Indian hemp is exceedingly variable, in some cases small doses producing alarming effects, in other instances the remedy seeming almost entirely powerless. There appears to be a very great difference in the susceptibility of persons to its influence; but this cannot explain the wide variance of the clinical results obtained by its use. A large proportion of the extracts upon the market must be inert. Possibly the crude drug undergoes deterioration during its long sea-voyage from India; at least I have had extract carefully made from genuine Indian hemp and offering all the physical characters of good extract, yet entirely inert in doses of many grains. I have seen an eighth of a grain of an English extract produce in a susceptible woman decided intoxication. So far as my present knowledge goes, although the foreign extracts of hemp are often inefficient, they are much more reliable than the American. The only way of administering hemp with satisfaction at present is for the practitioner to try various samples until he gets an active one, and then, being supplied with this, and having learned its proper dose by clinical experiment, to depend solely upon it. Hemp is not a dangerous drug; even the largest doses of its active preparations, although causing most alarming symptoms, do not compromise life. No case of acute poisoning by it terminating fatally has, that I am aware of, been reported. There is an officinal *tincture* (*Tinctura Cannabis Indicæ*, U.S.), the dose of which is thirty minims. The dose of the *fluid extract* (*Extractum Cannabis Indicæ Fluidum*, U.S.) is one minim.

Under the name of *tannate of cannabene* the German chemist, Merck, has put upon the market a preparation of cannabis, which is affirmed by Fronmüller (*Memorabil.*, 1882, 257) and by Hiller (*Berlin. Klin. Wochens.*, 1883, ix. 125) to be a very valuable mild hypnotic in doses of from four to seven grains. Fronmüller believes the failure of others to obtain similar results is largely due to the use of insufficient doses.

CLASS VII.—MYDRIATICS.

IN the present group are considered three medicines,—belladonna, hyoscyamus, and stramonium,—whose preparations, when given internally or applied locally to the eye, dilate the pupil, or, in other words, produce mydriasis, and whose action upon the system appears to be almost identical.

BELLADONNÆ FOLIA—BELLADONNA LEAF. U.S.
BELLADONNÆ RADIX—BELLADONNA ROOT. U.S.

The leaves and root of Atropa belladonna, an herbaceous perennial, a native of Europe, but cultivated in this country, and attaining a height of some three feet. The oval, pointed, entire, smooth, unequal leaves are in pairs, on a short footstalk. The bell-shaped, axillary, pendent flowers are of a dull reddish color. The globular berry is about three-quarters of an inch in diameter, deep purple, with a violet-colored juice, and adherent, green calyx. The dried leaves have a faint narcotic odor, and a sweetish, sub-acrid, slightly nauseous taste. The dried cylindrical branched root is from one to several inches in diameter, much longer, fibrous, externally reddish brown, internally whitish, almost odorless, with a very feeble sweetish taste.

ATROPINA. U.S.

The sole active principle of belladonna, discovered by Mein in 1831 and independently by Geiger and Hesse in 1833, occurs in silky prismatic and acicular, often aggregated crystals, of a bitter, burning taste, without odor, soluble in three hundred parts of cold and fifty-eight of boiling water, forty of benzole, thirty of ether, three of chloroform, and eight of alcohol. It is most abundant in the root, and, according to M. Lefort (*L' Union Médicale*, Nov. 1871), in that of young plants. Cyanogen gas passed through its alcoholic solution makes a deep-red (Hinterbeyer). The most reliable test is the physiological one,—*i.e.*, the production of mydriasis in a rabbit or a cat by the local application to the eye. It has been found in all the tissues of poisoned individuals, but always exists in greatest abundance, and is most easily demonstrated, in the urine.*

PHYSIOLOGICAL ACTION.—When the smallest physiological dose of atropia is administered to man, the only symptom induced is dryness of the throat and mouth, and possibly some disorder of vision. When a little larger amount is given, this dryness is more intense, and is associated with redness of the fauces, dilated pupils, disordered vision, and possibly diplopia. The pulse is sometimes at first rendered less frequent, but this decrease is very transient, and certainly in many cases cannot be demonstrated at all. Often from the first, certainly after a short time in all cases, the heart's beats, after a large dose of the alkaloid, become excessively rapid, the pulse rising to one hundred and twenty, or even one hundred and sixty; and in a little while a peculiar bright-red flush appears on the face and neck, and may spread over the whole body. As I have seen this, it lacks the punctations of the rash of scarlet fever, and is only in very severe cases followed by desquamation.

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* For a chemico-physiological study of *tropin* and other derivatives from atropia, see *Archiv Exper. Pathol.*, Bd. v., 463.

Early in the course of the symptoms of atropia-poisoning there is very often forcible expulsion of urine, and erections of the penis may occur; but afterwards there is very generally, Harley says always (*Old Vegetable Neurotics*, p. 207), retention of urine. With the symptoms above enumerated, intellection may remain perfect; but there are generally some lightness of head, giddiness, and confusion of thought, as well as a staggering gait and restlessness. Occasionally, even with doses which may be called medicinal, there are spectral illusions. Drowsiness is not a general or at all characteristic symptom: if present, it is apparently always produced indirectly, as by the removal of some cause of previous wakefulness. When a decidedly poisonous amount of belladonna or its alkaloid has been taken, all the symptoms already noted are intensified, and to them is added a peculiar talkative, wakeful delirium, in which the patient lives in a world of his own, engrossed by the spectres and visions which throng him, and completely oblivious to the surrounding realities. Thus, I have seen a lady remain for a long time stooping and holding fast to the bed-post, to which she talked in the most voluble manner, as though it were an intelligent living entity. Sometimes this delirium is wild, and the patient almost uncontrollably violent. After a time, sleep may come on, and on waking from this complete consciousness may be regained, or the symptoms may gradually subside. After a very large dose has been taken, severe convulsions may appear in a very short time, and persist, with or without furious maniacal delirium, until near death. Sooner or later, however, the delirium subsides into stupor, and the convulsions into paralysis; and when the dose has been enormous, and especially when the alkaloid itself has been taken, stupor, with great muscular relaxation, may occur very early. Lividity of the face, and evident imperfect aeration of the blood, are not seen in atropia-poisoning, except in the stage of most imminent peril. Death is preceded by marked failure both of the heart's action and of the respiratory forces. In most cases, I think, it is actually brought about by asphyxia.* Post-mortem examinations have shown in fatal cases congestion of the lungs, often with ecchymoses, and a similar state of the membranes and even substance of the brain and cord. According to M. Lemattre,* congestion of the retina is an almost characteristic lesion of atropia-poisoning.

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* See a case reported by S. W. Gross, *American Journal of the Medical Sciences*, 1869, p. 401, as a striking instance.

Upon the lower animals belladonna to a great extent acts as upon man, although its influence is much less powerful in them, and very much larger doses are required. Seeming differences of action are in most cases simply apparent, not real. Thus, in the dog, as in man, the pulse-rate is very greatly increased by atropia, whilst in the rabbit it is not. As will be shown hereafter, the rise of the pulse-rate in the former is largely due to paralysis of the par vagum. Now, atropia paralyzes the par vagum in the rabbit as much as in the dog, but in the rabbit pneumogastric paralysis, by section or otherwise, is never followed by a rise of the pulse-rate at all comparable to that seen under similar circumstances in the dog. Evidently the action of the drug is identical in the two cases, although the symptoms are different. In their sensitiveness to atropia animals differ very much, and, as a general rule, herbivora are less susceptible than carnivora. Thus, the rabbit may be fed for days entirely upon belladonna-leaves without injury, and many grains of atropia are necessary to kill him. Birds—at least pigeons—I have found will often recover after the hypodermic injection of two grains of atropia, and three grains by the mouth did not prove fatal. A very curious and at present inexplicable fact, which I have repeatedly verified, is that the pupils in pigeons cannot be dilated by the use of belladonna.

The close study of the physiological action of atropia can only be made system by system, and I shall now consider the subject under such headings.

Action on the Circulatory System.†—In the dog and in the rabbit small doses of atropia cause an increased frequency of the pulse, with rise of the arterial pressure. If, however, larger amounts of the alkaloid are used, and especially if the poison is thrown immediately into the venous circulation, there is an immediate fall of the blood-pressure, although the pulse increases as before. Bezold and Bloebaum (*Ueber die physiologischen Wirkungen des Schwefel-Atropins*, in *Untersuch. aus d. Physiolog. Laborator. in Würzburg*, Heft i.) state that the dose of atropia can be so graduated as to produce at first a temporary rise of the arterial pressure, followed in a short time by a fall.

In atropinized animals, as is stated both by Bezold and Bloebaum (*loc. cit.*, p. 33) and by Meuriot (*De la Méthode physiologique en Thérapeutique et de ses Applications à l'Etude de la Belladone*, Paris, 1868, p. 73), and as I have frequently seen, section of the vagi is not followed by any increase of the heart's action, and galvanization of the nerve is incapable of influencing the viscus. It follows that atropia in toxic doses paralyzes either the trunk or peripheral filaments of the nerve, and, as Bezold and Bloebaum believe, most probably the latter. The observers just alluded to have found that if atropia be injected into the carotid so as to reach the pneumogastric centres before the periphery, there is an instantaneous fall in the rate of the heart's beat,—an indication that upon the cardiac inhibitory centres atropia acts as a direct stimulant, precisely as it does on the spinal cord, the reason that the action is not more manifest under ordinary circumstances being the incapacity of the paralyzed vagus to transmit the central impulse. This asserted stimulation* of the inhibitory centre, if it be correct, accounts very beautifully for the primary brief slowing of the pulse stated to occur in some cases of atropia-poisoning. (See *Stillé's Therapeutics*, vol. i. p. 725. Mitchell, Keen, and Morehouse found it in about one-third of the cases after large hypodermic injections; Da Costa in a larger proportion, *Amer. Jour. Med. Sciences*, July, 1865; Miss Mary Putnam in some cases, *New York Medical Record*. 1873.)

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* Quoted by Tardieu, *Sur l'Empoisonnement*, Paris, 1867, p. 752.

† A long paper upon Calabar bean and atropia has been published by Rossbach and Fröhlich (*Verhandlungen d. Würzburger Phys. Med. Gesellschaft*, 1873), in which results totally at variance with those of all other observers, and many of them as totally at variance with general physiological laws, have been reached. Space cannot be spared for a criticism of this paper, and the reader is referred to the memoir itself abstracted (*London Med. Rec.*, i.) and to the critique of Harnack (*Archiv Experim. Pathol. Therap.*, ii. 307). See also *Pharmakolog. Untersuch.*, Bd. i. Heft 3 and 4.

The reports as to the action upon the frog's heart are somewhat at variance, Bowditch and Luciani having noted an increase, Gnauck a lessening in the cardiac pulsations (*Verhand. Physiolog. Gesellsch. zu Berlin*, 1881). H. Schapiro states that this variance is accounted for by the fact which he has discovered, that whereas at high temperature (15° C.) the pulsations are diminished, at low temperature (7° C.) they are increased. The frog's heart appears always to suffer final diastolic arrest, and cannot be re-excited by galvanic or other stimuli; and Bezold and Bloebaum (*loc. cit.*, p. 48) have found that the same thing occurs when an overwhelming dose of the alkaloid is injected into the jugular vein of a mammal. When, by the division of the spinal cord and vagi, the heart is isolated from the nerve-centres and the vaso-motor nerves are paralyzed, Bezold and Bloebaum have found that atropia, in minute as well as in large amount, lessens at once the arterial pressure. From these facts it follows that upon *the heart itself atropia acts as a direct depressant poison*, but for this influence to be apparent a very large amount of the alkaloid must be used.

From what has already been said, it is evident that the increase of the pulse seen in atropia-poisoning is in a measure due to paralysis of the cardiac inhibitory nerves; but that this is not the only cause is shown by the fact noticed by Lemattre (*Archives Générales*, August, 1865) and confirmed by my own experiments, that after section of the par vagum atropia still causes an increase in the rapidity of the heart's action. Further, Bezold and Bloebaum have found (*loc. cit.*, p. 54) that when the thoracic sympathetic is galvanized, even after large doses of atropia, the heart is very sensibly affected. From these facts it is obvious that atropia acts on the cardiac *accelerator nerve-centres*, or *possibly nerves*, *as a stimulant*, and, unless it be in lethal doses, does *not destroy* the *excitability* of these nerves.

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* The experiments and conclusions of Rossbach and Fröhlich confirm the existence of this stimulating action of atropia on the inhibitory centres, but cannot be received as correct, for reasons already given. Harnack (*Archiv für Exper. Pathol. und Therapie*, ii. 328) finds that the minutest dose of atropia increases the rapidity of the heart after stimulation of its inhibitory centres by muscarin and consequent slowing of its beat. This does not, however, prove that atropia has no action on the inhibitory centres. Further investigation is necessary for a positive conclusion.

The relation of belladonna to the *vaso-motor* nervous system is of such practical importance that it deserves the closest study. Brown-Séquard says positively that the drug has the power of exciting the muscular fibres of the arterioles; but, as he nowhere details the reasons for this opinion, I think little weight is to be attached to his statement. In 1857, Wharton Jones, of England (*Medical Times and Gazette*, p. 28, 1857), announced the fact (confirmed by Lemattre, *loc. cit.*, p. 52) that if atropia be dropped upon the web of a frog's foot, under the microscope the vessels can be seen to contract. Dr. Hayden (*Dublin Quarterly*, Aug. 1863) in repeating these experiments found that, if the skin were cut just above the foot, no contraction occurred, and concluded that the phenomenon was purely reflex. Meuriot (*loc. cit.*, p. 39) has obtained in some cases, but not invariably, the results of the last observer. He has, however, discovered that if the nerves of the leg be divided, no contraction ever takes place. Atropia is an irritant, and it is evident that the contraction caused by its local application is simply, as Hayden believed, a reflex phenomenon, precisely similar to that which occurs on the application of any chemical or mechanical irritant. The experiments of Wharton Jones, upon which so much has been based, must, therefore, be eliminated from the evidence on the question. The problem can be solved only by studying the effects of the remedy administered so as to act on the part solely through the circulation. Meuriot, as the result of such studies on the frog's web, has concluded that there is in the first stages of the poisoning a very slight contraction of the vessels, amounting to nothing more than increase of their tonicity; never to any decided lessening of their lumen. Dr. Harley (*The Old Vegetable Neurotics*, London, 1869, p. 220) has witnessed a more decided contraction of the vessels. I have tried the experiment several times, but obtained no decided results. On the other hand, Bezold and Bloebaum (*loc. cit.*, p. 50) have made similar experiments upon the ear and mesentery of the rabbit, and have never been able to detect any contraction of the vessels, and consequently deny its existence. In these experiments it was not possible to use the microscope,—which detracts greatly from their value.

The evidence derived from direct observation of the capillaries seems to me to be, on the whole, decidedly in favor of their contraction by minute doses of belladonna. I do not think, however, that much weight is to be attached to evidence of this nature. The alterations in the calibre of the vessels are so slight as to leave great play for the imagination of the observer, —a source of fallacy which probably accounts for the different results tained by different investigators. Much more decisive proof is, however, obtainable from a study of the arterial pressure. I have found that after section of the vagi atropia still has the power of raising very materially the arterial pressure. As atropia does not augment the force of the individual cardiac beat, and as the increase in the number of the cardiac pulsations caused by it after section of the vagi is comparatively slight, it is exceedingly probable that the rise of arterial pressure just spoken of is due to a contraction of the small vessels. This logical conclusion becomes almost a certainty when it is further known that after division of the cord, and consequent separation of the vessels from their vaso-motor centres, atropia is powerless to produce rise of arterial pressure, a fact vouched for by Bezold and Bloebaum, and which I can confirm from my own experiments (*Amer. Jour. Med. Sci.*, April, 1873). To this cumulative evidence must be added the experimental fact noted by Bezold and Bloebaum, that when a small dose of atropia is injected into the carotid artery—*i.e.*, into the vaso-motor centres—there is an instantaneous rise of blood-pressure.*

Viewing all these facts together, I am forced to give assent to the proposition that *atropia, in not too large amount*, is a *stimulant to the vaso-motor centres;* a conclusion in harmony with the action of the drug on all the other motor centres. All observers agree that in the advanced stage of atropia-poisoning, after the blood-pressure has commenced to fall, there is dilatation of the capillaries. It seems most probable that this is due to a direct action of the poison on the muscular fibres in the coats of the vessels; for when directly applied to the web of the frog's foot, atropia, after a time, produces an evidently paralytic dilatation; and Bezold and Bloebaum have found that the arterial muscular coats in atropia-poisoning finally lose their irritability, but that so long as they retain it, galvanic stimulation of a sympathetic nerve does not fail to induce contraction in the tributary vessels.

Action upon the Nervous System.—The delirium which is so characteristic of atropia-poisoning shows that it has especial relations with the cerebral cortex. Prof. Albertoni has made a series of experiments to determine whether it inhibits or affects the motor powers of the cortex. He finds that neither the single large dose nor the repeated continuous dose has any power in preventing the epileptic seizure resulting in dogs from the stimulation of the motor zone of the cortex: enormous toxic doses seem only to render the response slower and less vivid (*Arch. Exper. Path. und Therap.*, xv. p. 265).

In 1862, Dr. S. Botkin (*Virchow's Archiv*, Bd. xxiv. p. 85) found that when the vessels of a frog's leg were tied and the animal poisoned with atropia, whilst paralysis developed itself in the ordinary way in the uninjured leg, the injured leg preserved its motility. He also discovered that the nerve of the leg whose artery had been tied transmitted a forcible impulse to its tributary muscles under the stimulus of a galvanic current much weaker than could elicit the faintest response from the nerve of the opposite side. He concluded, very logically, that atropia acts as a paralyzant to the motor nerve-trunks themselves, and also, since motion persisted in the protected leg after it was completely lost in its fellows, that this influence of the drug was exerted upon the motor trunks before the spinal centres. These experiments have been confirmed by Lemattre (*loc. cit.*, p. 49), by Bezold and Bloebaum (*loc. cit.*, p. 20), by Meuriot (*loc. cit.*, p. 90), and by Fraser and others, who have proven that atropia, if in sufficient dose, has the power of *destroying the excitability of the efferent or motor nerve fibres*, but that it must be in very large quantity, so that in mammals death may be caused by the alkaloid and yet a notable amount of functional power be retained by the motor nerves. Bezold and Bloebaum, whose elaborate experiments are especially commendable, affirm that very rarely have they been able totally to destroy by atropia the functional power of the motor nerves, and also have shown that both the nerve-stem and the peripheral intra-muscular nerve-endings are affected. All the experimenters agree that no stage of super-excitability preceding that of depression can be discovered.

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* It is proper to state that Bezold and Bloebaum attribute this rise to psychical disturbance, without, however, as it seems to me, good reason.

Prof. Thos. R. Fraser discovered in 1869 (*Trans. Roy. Soc. Edinb.*, xxv. 450) that if a frog receive an injection of about one-thousandth part of its weight of atropia, a condition of perfect paralysis and abolition of reflex action comes on after a time, and lasts from two to four days, to be succeeded by a tetanic stage, with violent convulsions and excessive excitability of the reflex centres. The convulsions of this stage have been shown by Fraser to be spinal, occurring after section of the cord in all parts of the body. Dr. Fraser found (Exp. 59, p. 481) that when he protected the hind legs by tying the aorta at its bifurcation, tetanus appeared in them at a time when the anterior legs were completely paralyzed and the brachial nerves were unable to respond to the galvanic stimulation. Again, he was able to produce symptoms closely analogous to those caused by atropia by injecting simultaneously two poisons,—one a stimulant to the cord, the other a paralyzant of the nerve-trunks. These facts would seem to prove that during the paralytic stage of the action of atropia a convulsant condition of the cord is masked by a paralyzed state of the efferent nerves. This conclusion is, however, invalidated by certain facts observed by Fraser, and especially by the recent researches of Ringer and Murrell. Thus, in some of Fraser's experiments the paralysis was at no time sufficient to mask a tetanus; in experiments of all three observers the tetanus did not develop at once in parts in which the nerve-trunks were protected by cutting off their blood-supply; contrary to the observation of Fraser, in a number of experiments performed by Ringer and Murrell, after the aorta had been tied tetanus developed no earlier in the protected than in the unprotected leg. In some of the experiments of Ringer and Murrell the paralyzant effect of the poison passed off—voluntary and reflex action returning—before the supervention of the tetanus. These facts *seem* to show that the paralysis as well as the tetanus are due to an action upon the centres, the drug so acting upon the spinal cord as first to abolish and then intensify its reflex activity. The explanation of this singular action cannot at present be considered as established. Drs. Ringer and Murrell believe that both the paralysis and the tetanus are due to a depressant action. The theory is that the normal cord has a power of resisting impulses received from the periphery, and especially of preventing their wide propagation among the spinal centres. During the first stage of the atropia-poisoning it is supposed that the motor portions of the cord are so paralyzed as to be unable to form or propagate any motor impulse, and hence the general paralysis. Later on, however, the motor cells have so far recovered themselves as to be able to generate impulses freely, although the resistive power of the cord is still in abeyance. Consequently a peripheral impulse plays, as it were, at will, up and down the spinal cord, and instead of giving rise to a simple reflex action, gives origin to a series of reflex movements, involving all the muscles, and constituting a tetanic convulsion.

The experiments of Lemattre (*loc. cit.*) indicate that belladonna exerts a similar paralyzant and convulsant action in mammals, and Dr. Fraser's investigation confirms this. It would seem, however, that in mammals the convulsant action comes on more rapidly, and is less protracted, and that the paralyzant action is also less intense, than in the frog; so that whilst the batrachian poisoned by atropia is in the beginning paralyzed and afterwards convulsed, the mammal suffers from convulsions and reflex spasms early in the poisoning, and often exhibits evidences all through of the excited reflex activity. The difference in the action of non-fatal doses of atropia upon the frog and upon the mammal is graphically expressed by the diagrams on the following page, which are copied from the paper of Dr. Fraser.

Fig. 1 represents an experiment made upon a dog: in it the curve of paralysis, op_1 p_2, leaves the line of normality, AB, before the curve of spinal stimulation, the first symptoms being those of paralysis. As the curve of op_1 p_2 never reaches the line of complete paralysis, CD, the paralytic action is not sufficiently great, in the height of the poison, to prevent the manifestation of the considerable spinal stimulant action.

FIG. 1.

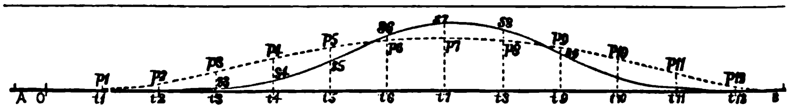

FIG. 2.

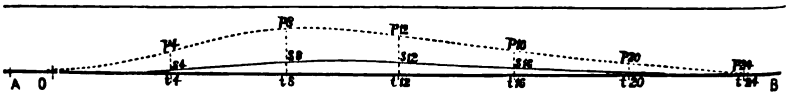

Fig. 2 expresses the results of an experiment upon a frog: in it, although there was some spinal stimulant action, as evinced by the curve s_4, s_8, s_{12}, s_{16}, and although the paralytic curve p_4, p_8, p_{12}, p_{16}, p_{20} never reaches the line of complete paralysis, CD, yet it is manifest that the paralytic action of the drug throughout the experiment masks and covers up the convulsive influence.

It is very certain that in man atropia exerts this double influence; for the records of poisoning cases are at once the records of convulsions and of paralysis. It would seem that early profound paralysis occurs when a very large dose of the poison has been taken in its concentrated alkaloidal condition, and consequently has been rapidly absorbed and suddenly precipitated upon the nervous system.

In the experiments of Botkin, made by tying the vessels of the frog's legs, as described on page 236, the investigator found that although for a time irritation of the foot of the perfectly paralyzed leg would cause spasms in the opposite limb whose nerve was protected, yet later in the poisoning, although irritation of the foot of the protected leg caused movements in that leg, no irritation of the opposite poisoned foot was able to induce any response whatever on either side. From this he drew the inevitable conclusion that, whilst atropia paralyzes first the motor nerves, yet later it acts also on the afferent nerves. The very beautiful experiments of Dr. Fraser, already quoted, certainly show that the afferent nerves enjoy a comparative immunity from the influence of atropia in large doses. For when one leg of a frog was protected by tying the crural artery during the period of general paralysis, any irritation of the poisoned leg would produce immediate reflex convulsions in the unpoisoned extremity,—a demonstration that whilst the functions of the efferent or motor nerves were suspended wherever the poison reached, the afferent nerves retained more or less of their activity. This of course confirms a portion of the experiments and conclusions of Botkin, and does not disprove that atropia acts to some extent upon the afferent nerves; for a very feeble impulse reaching the cord in its excited condition would cause reflex movements. Bezold and Bloebaum (*loc. cit.*, p. 20) have investigated this subject by exposing the sciatic nerves of a strychnized frog, immersing them for a portion of their course, the one in a solution of atropia, the other in a solution of the phosphate of sodium, and then testing the effect of the application of stimuli in causing reflex movements. The result was not very satisfactory, so many sources of fallacy arising—sources not necessary here to point out—as to vitiate greatly the experiments. They certainly found, however, that the nerve-trunk preserved for some time its power of transmitting impulse even when immersed in a two-and-a-half per cent. solution of the alkaloid. Bezold and Bloebaum (p. 25) also repeated the experiments of Botkin, substantially confirming them, but showing that very large doses are necessary to affect seriously the conducting powers of the afferent nerves.

The following experiments of Meuriot (*loc. cit.*, p. 95) prove conclusively that atropia does influence the afferent nerves. He found that if a frog be bound tightly around the body so as to interrupt the circulation, and then be poisoned by atropia in the front part of its body, at first irritations in any part give rise to general spasms, but after a time in order to get any movements of the hind legs it is necessary to apply an irritant to them. Again, the hinder parts of a frog were so bound by ligatures as to cut off on the one side all communication except by the nerves, and on the other to leave free the nerve and the vessels. A strong injection of atropia was then given, and when the moment came that irritation of the periphery of the leg whose circulation was free would no longer cause reflex spasms, the artery of this leg also was tied, so that both legs, the one atropinized, the other not, were now connected with the body of the frog only by their nerves. Strychnia was given hypodermically, and it was found that, whilst irritation of the atropinized leg had no effect, stimulation of the non-atropinized leg gave rise to general convulsions. The whole present evidence shows that *atropia depresses the afferent nerves, but much more feebly than it does the efferent nerves.* Miss Mary Putnam (*N. Y. Med. Rec.*, 1873) asserts that if the general tissue of the frog's limb be tied, the vessels and nerves being left intact, so as to prevent diffusion of the poison through the cellular tissue, the sensitive nerves are alone affected by atropia. As no details of experiments are given, the matter rests simply upon the assertion of Miss Putnam. It is very difficult to imagine why a nerve should be affected differently by a poison when reaching it by different routes, and equally difficult to conceive how the poison should reach more effectively the motor than the sensitive nerves by diffusion. Further, it is also almost as unreasonable to believe that any perceptible diffusion through the cellular tissue should occur when the seat of injection is in a distant part of the body. Taking together the facts that Miss Putnam's assertion is unsupported by detailed experiments, is exceedingly improbable, and is seemingly opposed to an enormous mass of experimentation by some of the most experienced and able investigators who have ever lived, it seems to me that it cannot be accepted. It is probable that atropia acts upon the peripheral filaments of the nerves more quickly than upon the main trunks; this is corroborated by Miss Putnam, who states that she has seen galvanization of a sciatic nerve cause indications of pain in an atropinized animal when the peripheral sensation was already lost.

There can be no doubt that in the higher animals atropia acts upon the cerebrum as it does in man, producing the same peculiar delirious intoxication often ending in stupor. It is not necessary to discuss this matter further, except to remark that belladonna is *not* a hypnotic. The fact that the exhibition of a remedy is followed by sleep in disease is no proof that the remedy is in a proper sense a hypnotic. No one would give oyster soup such a cognomen, yet in certain exhausted wakeful states of the system such food may bring back sound sleep. If belladonna ever acts as a hypnotic, it is in this indirect way, by removing some cause of abnormal wakefulness. It can never be relied on, like opium, to induce sleep.

Action on the Voluntary Muscles.—The voluntary muscles escape un scathed in atropia-poisoning. It is true that Lemattre has shown that the contractility of a striated muscle may be destroyed by soaking it in a very concentrated solution of the alkaloid; but long before any such action can take place in life the animal is killed; consequently after death from belladonna the contractility of the voluntary muscles is found unimpaired.

Action on the Abdominal Canal.—On the non-striated muscles the action of the drug is pronounced, but its exact nature is uncertain. Meuriot states (*loc. cit.*, p. 112) that if the belly of an animal poisoned by atropia be opened, the intestines will be found undergoing violent contractions, and that belladonna is a powerful excitant of the non-striated muscles. On the other hand, Bezold and Bloebaum affirm that they have experimented upon the intestines, bladder, uterus, and ureters, and that in all cases there is a state of marked sedation from atropia, and that, whether a small or a large dose be used (*loc. cit.*, p. 65), there are produced muscular quietness and relaxation in all these organs,—evidences of sedation not preceded by any stage of excitement, and always accompanied by lessening of the electro-muscular sensibility. They state, further, that by the use of sufficient doses absolute muscular paralysis of the organs alluded to is induced, so that the strongest faradaic currents are unable to cause any motion. P. Keuchel (*Das Atropin und der Hemmungsnerven*, Inaug. Diss., Dorpat, 1868) has made a most elaborate series of experiments to determine the effect of atropia upon the inhibitory fibres of the splanchnic nerve. It has been shown by Pflüger that galvanization of the peripheral ends of the divided splanchnics causes immediate arrest of the peristaltic intestinal movements, and, although the subject has not been absolutely worked out, it is almost certain that some of the splanchnic fibres are the inhibitory nerves of the intestinal coats. Keuchel has found that even when doses of atropia so small as not to affect distinctly the motor nerves are given, galvanization of the splanchnics fails to influence the intestines, whose vermicular movements are still active, and therefore that atropia paralyzes the peripheral inhibitory intestinal apparatus precisely as it does that of the heart. There is, of course, a seeming disagreement between these researches and those of Meuriot and of Bezold and Bloebaum; and the apparent confusion is increased by the assertions of Dr. I. Ott (*New York Med. Journal*, 1883, 170), that minute doses of atropia prevent the production of peristalsis by salt placed upon the intestine, whilst large doses exaggerate the action of the salt. It would appear from this that atropia first stimulates, then paralyzes the intestinal inhibitory nervous system. Before the question can be settled further researches are necessary, but it is possible that all these observers saw and reported correctly, the differences being the result of varying doses. It appears certain that, in full doses, atropia paralyzes the smooth muscular fibres of the intestine, bladder, etc., and it may be that in any dose it depresses their activity directly, but that, by paralyzing more quickly the inhibitory apparatus, it sometimes places the intestinal muscular coat in such a position that it will respond [illegible] and also that very minute [illegible] This view is [illegible] Kenchel was 0.075 gr.; [illegible] the rabbit. When Ott [illegible] Kenchel.

[illegible] been stated that in [illegible] whereas large doses [illegible] and the acceleration takes place [illegible]—a proof that it is due to [illegible] the medulla. (Bezold and [illegible] doses are administered, [illegible] the peripheral pneumo-[illegible] respiration: for if in [illegible] vagum be cut, respi-[illegible] has been more freely [illegible] by section [illegible] belladonna-poisoning, the [illegible] may become very dark, and [illegible] entirely from failure [illegible] of functional power [illegible]

[illegible] the earliest and most notable [illegible]

[illegible]

early, and in the later stages may be entirely suppressed.* Meuriot states that the secretion of urine rises and falls in atropia-poisoning with the arterial pressure. The experiments of Harley upon men (*loc. cit.*, p. 214) would appear to show that medicinal doses of atropia decidedly increase the solids of the urine, slightly the urea and uric acid, very markedly the phosphates and the sulphates.

In regard to the secretions of the alimentary canal, the action of atropia is very uncertain. It has been a matter of traditional and clinical belief that they were increased, and Harley gives some experiments which he claims corroborate this; Meuriot, on the other hand, states that they are lessened. I cannot find, however, any experiments that seem to me at all decisive; and clinical evidence certainly indicates that the alimentary secretions, if affected at all, are increased.

Action on Temperature.—In moderate doses atropia causes a pronounced rise in temperature, but in very large decidedly toxic amounts it lessens animal heat. Thus, in the dog, Meuriot has obtained an augmentation of from 1° to 3° C., and Duméril, Demarquay, and Lecomte† of 4° C. In fatal poisoning of the same animal, these observers have noticed a fall respectively of $5\frac{1}{10}$° and of 3°.† In man, Meuriot, in the use of medicinal doses, has observed the temperature to rise ½° to $1\frac{1}{10}$°, and Eulenburg† ½° to $\frac{8}{10}$°.‡ Harley has seen in man an elevation of 1° F. As pointed out by Meuriot, the rise and fall of temperature probably correspond to the rise and fall of the blood-pressure.

Summary.—From what has been already stated, it is evident that the action of atropia in therapeutic and in toxic doses is in a sense quite different.

In full medicinal doses it produces a sort of febrile state, with dryness of the mouth, increased rapidity and force of the circulation, quickened respiration, elevation of temperature, and secretion of febrile urine. The rapidity of the heart's action is due to paralysis of the peripheral inhibitory nerve and to stimulation of the accelerator nerves; the increased arterial pressure, to the increased cardiac action, together with the general contraction of the capillaries, the result of excitation of the vaso-motor centres. The spinal cord is not sensibly affected by these doses; the motor, and probably to a much less degree the sensory peripheral nerves, suffer lessening of functional activity, although the influence of therapeutic doses of atropia upon them must be very slight. If the dose be sufficiently large, the cerebrum is thrown into a condition of mild delirium, resembling also that of fever.

After decidedly toxic doses of atropia, the blood-pressure falls, from dilatation of the capillaries, owing to the paralysis of their muscular coats, and from direct laming of the heart-muscle. The temperature also falls; the muscular system is relaxed, and sensation is impaired, from the paresis of the motor and sensory nerves respectively; yet convulsions may now occur from the over-activity of the reflex centres, the predominance of paralysis or of convulsions varying with the dose, as the depressing or stimulating influence is the more powerful. Delirium precedes stupor, which in turn precedes death, from asphyxia, caused by failing trunkal nerve-functions, or very rarely from syncope, caused by failure of the cardiac muscle.

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* See poison-case reported by Dr. Gross (*loc. cit.*), also cases of Dr. Morer (*Annales de la Société de Médecine de Gand*, 1873).

† Quoted by Meuriot, p. 111.

‡ These figures are probably all of them Centigrade, though it is not stated by Meuriot.

Local Action.—It is evident that when belladonna is applied to a part it must act locally as a paralyzant, no doubt overpowering the capillary walls, the sensitive and motor nerves, and even muscular and glandular cell-action; for, except in the case of the latter, experimental evidence has already been brought forward to prove that, locally and freely applied, belladonna is a sedative poison, and clinical evidence points very strongly to its exerting a similar influence upon gland-cells. A. Zeller (*Virchow's Arch.*, lxvi.. p. 384) has found that a one per cent. solution of atropia brought in contact with the blood, outside of the body, has a decided influence in arresting the movements of the corpuscles.

Action on the Eye.—Atropia placed in the eye, or given internally, dilates the pupil of all animals except birds. Accompanying this mydriasis are paralysis of accommodation and a lessened intraocular pressure. In regard to the latter, the subject is so intricate that I must refer the reader to the treatises of specialists.*

Before discussing briefly the action of atropia upon the pupil, the fact that a recent American female writer has reasserted the old theory that the movements of the iris are due to erectile tissue, or, in other words, to its blood-vessels, seems to render necessary a few words as to the real motile power of the part. In the first place, it is an indisputable anatomical fact that the iris is largely composed of muscular fibres, and it is a simple common-sense deduction that the muscular fibres are there for the purpose of causing motion, especially since, in many animals, it can be readily demonstrated that whilst some of these fibres are circular, others are radiating, so that by position they become antagonistic. The paper of Dr. Arlt (*Archiv für Ophthalmologie*, 1869) seems to me very decisive. In a very elaborate series of experiments it was found that when the upper cervical ganglion was stimulated the pupil dilated long before any influence upon the vessels was detected, and that on cessation of the stimulation the pupil became natural long before the spasm of the vessels yielded; to my mind a proof that the ganglion has fibres other than vaso-motor,—fibres which control the muscular actions of the iris, and are more sensitive than the vaso-motor filaments; and, secondarily, a proof that the movements of the iris are not due to movements of the blood-vessels. Space cannot be afforded in the present work for a further discussion of this subject. The reader is respectfully referred for further information to books on the physiology of the eye, and especially to Engelhardt's paper, *Beiträge zur Lehre von den Bewegungen der Iris* (*Untersuchungen aus dem physiolog. Laboratorium in Würzburg*, zweiter Theil.)

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* See especially *Der intraoculare Druck und die Innervations-Verhältnisse der Iris.* Von Prof. Dr. Stellwag von Carion. Wien, 1868.

In considering the action of belladonna upon the eye, it is necessary to view separately its influence when applied locally and when given internally; and I shall consider these in the order in which they here stand.

It may be first asserted that the dilatation induced by the local application of belladonna or of its principles is a nervous phenomenon, and not due to a direct action of the drug upon the muscular fibres of the iris; for as all of these, both the radiating and the circular, are of the same nature (*non-striated* in mammals), their antagonism is simply due to position; and it seems inconceivable that mere position should affect the relations between a muscle and a drug. Moreover, decisive proof is afforded by the experiments of Bernstein and Dogiel, who found that whilst galvanic irritation of the oculo-motor nerve was unable to cause contraction of the pupil in the atropinized eye, yet when the electrodes were applied to the eyes in such a way as to affect directly the iris, contraction occurred,—phenomena only explainable by the theory that the nerve-endings were paralyzed, whilst the muscle was unaffected. Of the truth of this observation there can be no doubt, as it has been confirmed by Dr. G. Engelhardt (*Untersuch. aus dem physiolog. Laborat. in Würzburg*, Theil ii. p. 321).

The statement first made by Wharton Jones (*Medical Times and Gazette*, 1857), that the reason atropia does not dilate the pupils of birds is that their irides have no radiating fibres, has been disproven by the beautiful anatomical researches of Alex. Ivanoff and Alex. Rollett (*Archiv für Ophthalmologie*, vol. xv. p. 1), confirmed by Johannes Diegel (*Max Schultze's Archiv für Microscop. Anat.*, Bd. vi. Heft i., 1870). Although Prof. Donders (*The Accommodation and Refraction of the Eye*, Syd. Soc. ed., p. 584) says that the pupillary action of atropia "is slight in birds, in whom it was formerly overlooked," in my own experiments the most thorough application of very strong solutions to the eyes of pigeons has had no distinct effect. In previous editions of this book I ventured the surmise that the lack of action of atropia upon the irides of birds might be due to the muscle being of the striated type. According to the experiments of Szpilman and Luchsinger, this supposition is correct. In the œsophagus of the bird the muscle is non-striated, and atropia paralyzes it; in the œsophagus of the rabbit the muscle is striated, and atropia has no action; in the cat a portion of the œsophagus has smooth muscular fibres, a part striated, and the former is paralyzed, the latter unaffected, by the alkaloid (*Arch. f. d. Ges. Physiol.*, xxvi. 460).

The dilatation of the pupil by the local application of atropia* is certainly independent of any nerve-centres farther back than the ciliary ganglion. This is proven by the following facts: Claude Bernard (*Physiologie et Pathologie du Système Nerveux*, Paris, vol. ii. p. 212) and Lemattre (*loc. cit.*) both have found that atropia-mydriasis occurs in animals after section of the oculomotor, and I have seen it in cases of complete oculo-motor paralysis in man. It also takes place after section of the trigeminus or of the cervical sympathetic, or of both of these nerves, as is shown by the testimony of numerous observers and by my own experiments. In man, I have seen it after paralysis of the sympathetic (*Philadelphia Med. Times*, vol. i. p. 290). Not only is the dilatation of the pupil by the local application of atropia independent of the central nervous system, but also of the ciliary ganglion, and it is therefore due to an action exerted directly upon the *nerve-endings in the iris.* The experiments of Bernstein and Dogiel, confirmed by Engelhardt, already quoted, are in themselves almost enough to establish the truth of this proposition. More direct evidence is not, however, wanting. Thus, Vierordt* has found that atropia locally applied still causes mydriasis after the removal of the ciliary ganglion. Prof. I. Hoppe (*Die Nervenwirkungen der Heilmittel*, Leipsic, 1856, zweiter Heft, p. 179) has discovered, and Y. Valentin (*Versuch einer physiologischen Pathologie der Nerven*, Leipsic, 1864, zweite Abtheilung, p. 368) has confirmed, that in the eye of the frog removed from the body atropia will produce dilatation of the pupil. According to Borelli (*Edinburgh Medical Journal*, Nov. 1871), mydriasis is produced by the alkaloid when applied to the eye of a man just dead. Lastly, the presence of the alkaloid in the humors of the atropinized eye has been proven by numerous observers, among whom may be mentioned Lemattre (*loc. cit.*, p. 55) and Prof. Donders (*The Accommodation and Refraction of the Eye*, Syd. Soc. ed., p. 588), who have found that the liquids removed from such an eye are capable of causing dilatation of the pupil of another eye.

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* Contraction of the pupil before dilatation noticed in dogs (Reese) and rabbits (Rossbach and Fröhlich), is probably caused reflexly by irritant action of the atropia.

It having been demonstrated that the mydriasis of the atropinized eye is the result of an action upon the peripheral nerve-fibres, the question arises, Are the ends of the oculo-motor, the contractor of the pupil, paralyzed, or are the ends of the sympathetic, the dilator, stimulated, or is there a double influence, both of these actions occurring? Both Donders (*loc. cit.*, p. 589)† and Stellwag von Carion (*loc. cit.*, p. 92) insist that the paralysis of accommodation is proof of paralysis of the oculo-motor nerve, and it seems to me they do so with truth. However this may be, there is abundant direct proof that the oculo-motor fibres are paralyzed, since the experiment of Grünhagen, showing that galvanization of the exposed oculo-motor nerve does not affect the atropinized pupil, confirmed by Engelhardt (*loc. cit.*, p. 321), and by Rossbach and Fröhlich (*Pharmak. Untersuchungen*, Würzburg, i., p. 6).

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* Unfortunately, the only notice I have seen of this capital experiment is in Hermann's "*Grundriss der Physiologie.*" No reference is given, and I have been unable to find the original paper.

† See also Von Graefe, *Deutsches Klinik*, 1861.

In artificial mydriasis there is, then, undoubtedly peripheral palsy of the oculo-motor. The question arises, Is there also stimulation of the dilating nerve? ·The evidence as to this is not so positive, but to my mind indicates very strongly that there is such an action. Clinical experience certainly shows that the dilatation produced by a mydriatic is not merely a passive movement of relaxation, but is active, capable of tearing up inflammatory adhesions even when of some firmness. Again, the dilatation that occurs after the paralysis of the oculo-motor nerve in man and after its destruction in animals is not at all equal to that produced by atropia, and, indeed, can be largely increased by the action of the drug; further, in the eye separated entirely from the nerve-centres (see above) atropia still causes a wide dilatation; facts which necessitate the belief either that the alkaloid acts upon the sympathetic fibrillæ, or that the peripheral fibres of a nerve are in themselves nerve-centres, acting upon the muscle of themselves even when separated from their centres.

It has been urged against the view here taken that even the widest artificial mydriasis is increased by galvanization of the sympathetic. De Ruiter states the contrary; but, since Grünhagen, Hirschmann, and Engelhardt separately affirm as the result of personal experiment the correctness of the asserted fact, it must be accepted. Granting its truth, I do not think it warrants the deduction, since it is very conceivable that an agent may excite the peripheral filaments of a nerve very greatly, and yet not to that point that they are incapable of further excitation.

In conclusion, the action of atropia applied to the eye may be summed up as follows: the mydriasis is the result of a direct influence upon the peripheral nerve-fibres, those of the oculo-motor being certainly paralyzed, those of the sympathetic and its ally the trigeminus being probably excited.

In regard to the constitutional action of atropia, it is evident that when the alkaloid is administered internally there are only four possible ways in which it can cause mydriasis, and that these are as follows: 1. By acting alone on the sympathetic centres, as a stimulant. 2. By acting alone on the oculo-motor centres, as a paralyzant. 3. By combining these actions. 4. By being carried to the eye, and acting as though locally applied.

Authors are greatly at variance in their conclusions: thus, Harley (*The Old Vegetable Neurotics*) and Hayden (*Dublin Quarterly Journal*, August, 1863) may be cited as in favor of the first view, and Budge (*Ueber die Bewegung der Iris*, 1855), Braun (*Archiv für Ophthalmologie*, Bd. v. Abth. ii.), and Hirschmann (*Zur Lehre von d. durch Arzneimittel*, etc., *Reichert's Archiv*, 1863) as favoring the second. Neither the first nor the second view is, however, tenable: the first, because of a fact which has been asserted by authorities and which I have experimentally corroborated, namely, that atropia given hypodermically causes dilatation of the pupil after section both of the trigeminus and of the sympathetic in the neck; the second, for the reason that after section of the oculo-motor in animals, or after complete paralysis of the oculo-motor in man, the mydriasis is much less than that of atropia-poisoning.

In regard to the third view, I have noticed that the dilatation of the pupil under the constitutional action of the alkaloid after section of the cervical sympathetic is still greater than that which is normally produced by oculomotor paralysis. At my solicitation, Dr. T. G. Morton, of this city, cut down to the optic nerve in a rabbit and divided all the structures about it. The pupil contracted very much at the time; the cornea was not sensitive, but recovered its sensitiveness in part after some days. Atropia given hypodermically dilated the eye very markedly, but not nearly to the extent of the other eye. If in this experiment all the ciliary nerves were really cut, the proof is conclusive that the mydriasis is not of centric origin; the reason that the pupil did not dilate so freely as the other being the strong contracting influence it was under, and the great reduction in the amount of blood, *i.e.*, the amount of atropia, entering the eye, owing to the division of the blood-vessels.

An experiment of Lemattre, if it be accurate, is also conclusive in proving that the action of the mydriatics upon the pupil, even when administered internally, is a peripheral one. He succeeded in producing mydriasis in normal eyes by placing in them aqueous humors taken from dogs poisoned with atropia, and even from a fœtus whose dam had been killed by the alkaloid. Donders, however (*loc. cit.*, p. 589), failed to get the dilatation; and two or three experiments have yielded me the same negative result. It requires no elaborate argument to prove that in this case a negative result does not overpower a previous positive one: still, the experiments of Lemattre need confirmation. In the Pennsylvania Hospital, under the care of Dr. Morton, not long since I saw a man who had been wounded by a railroad accident in such a way that the whole of the temporal bone anterior to the petrous portion was thrust into the side of the head; there was complete paralysis of the facial, of the trigeminus, and of the oculo-motor, as could be readily demonstrated upon the man, who lived some months, finally dying suddenly of abscess of the brain. The carotid canal was so pressed upon that the sympathetic, which passed upwards through it to the eye, must have also been paralyzed. The eye was, as proven by the autopsy, separated from all connection with the nerve-centres, and yet when atropia was given hypodermically the pupil dilated. The proof seemed complete that the mydriasis was owing to a peripheral action.

Our knowledge of the action of atropia upon the pupil may be summed up as follows: Atropia applied locally causes mydriasis by paralyzing the peripheral ends of the oculo-motor nerve, and probably by stimulating the peripheral ends of the sympathetic. Atropia given internally *almost* certainly causes mydriasis, not by influencing the nerve-centres, but by being carried in the blood to the eye itself, and there acting precisely as when applied locally.

THERAPEUTICS.—The results of clinical experience are in strict accord with what is known of the physiological action of belladonna. The chief indication for its use is *to relax spasm.* In the case of voluntary muscles its powers are comparatively feeble, except when it is *thrown directly into the muscle affected.* In this manner Dr. S. Weir Mitchell (*Injuries of Nerves*, Philadelphia, 1872, p. 258) has obtained very marked relief in the fearful spasms following nerve-wounds, and Dr. J. M. Da Costa in rheumatic spasm (*Pennsylvania Hospital Reports*, 1868). The benefit derived in this way is evidently due to the depressing effect of the drug upon the terminal nerve-filaments, with which it comes in direct contact, and to a certain extent also on the muscle itself. When given by the mouth, so small an amount of the remedy reaches the diseased part as scarcely to affect it, and very little or no relief follows. As has been previously shown, the non-striated muscles are more affected than the striated by belladonna, and clinically the drug is found to be even more efficacious in *spasm* of the *involuntary* than of the voluntary muscles: in such cases it is often of value used internally. It must be thus administered in *lead colic*,—in *simple spasmodic colic*,—in *spasmodic dysmenorrhœa*,—in *spasmodic constriction* of the *bowels* with *obstinate constipation*,—in *laryngismus stridulus*,—in *nervous cough*,—in *asthma*,—in *hiccough*,—in *whooping-cough*,—in which, as originally advised by Bretonneau, it has been largely used, and is one of the best known remedies; also, even in the spasms accompanying passage of *renal* and *biliary calculi*, where of course it often fails. Wherever it is possible, however, it should be used locally in spasm of the involuntary as well as of the voluntary muscles. Thus, in *spasm* of the *urethra*, the ointment should be rubbed in along the canal; in *rigid os uteri*, the extract should be applied directly to the os; in *asthma*, belladonna should be inhaled, either by means of the cigarette or of the atomization of a decoction of the leaves; in *spasm* of the *sphincter ani* from *fissure* or other cause, it should be applied directly to the part by poultice or ointment.

It is, no doubt, by relaxing spasm, or rather by lessening irritability, that belladonna acts in that form of *incontinence* of *urine* which is seen generally in children. It has been taught that this affection is due to a relaxation of the sphincter, but undoubtedly in the great majority of cases its real cause is an irritability of the bladder itself, so that spasmodic contraction occurs under the stimulus of a small portion of urine. A common result of the ingestion of a large dose of belladonna is a paralytic retention of urine, due no doubt to the local action of the atropia in the urine upon the bladder. It is needless to point out more in detail how the indications in incontinence are met. In these cases the drug must be given in as large doses as the system will bear, and the impression should be maintained for weeks Usually the dose has to be steadily increased. Under the present indication also probably belongs the use of the remedy in *constipation.* In doses of one-quarter to one-half grain of the extract, added to a laxative pill, belladonna is of great service, and sometimes used alone will cure chronic constipation. It appears to be of most value in subjects of rigid tone; in feeble, relaxed people, strychnia is preferable.

To relieve Pain.—Physiologically viewed, atropia should be of little value for this purpose; and I think clinical evidence bears this out. Dr. Mitchell has had probably the best opportunities ever afforded for testing this, and he says decidedly that it is of little use in severe suffering. My own experience is to the same effect. There is, however, considerable evidence of its value in *neuralgia*, but it is chiefly as to its efficiency when injected immediately in the neighborhood of a painful nerve, or applied as inunction over its course when superficial. In large quantity, belladonna certainly affects the afferent nerves, and, used as above, may readily relieve pain. It is very probable also that at times it cures neuralgia by modifying the circulation in the affected part. Though these things be so, yet belladonna is almost immeasurably below opium as an analgesic. In some forms of *neuralgia* with *spasm* it is of service by a double action.

To impress the Heart and Blood-Vessels.—Under the idea of its contracting the blood-vessels, belladonna has been highly commended by Dr. Harley (*loc. cit.*) in *pneumonia*, acute *nephritis*, and various other acute diseases. I have had no experience with it in these affections, but the published accounts do not seem to me to indicate that it is of equal value with other remedies or combinations of remedies. In chronic albuminous nephritis I have tried it, as recommended by Dr. Harley (*loc. cit.*), but have failed to derive any advantage from it. In *ordinary sore throat*, it does good by acting upon the blood-vessels, and by relaxing the pharyngeal muscles. It may possibly be of use given before the administration of chloroform, to prevent cardiac inhibitory arrest. (See *Brit. Med.*, 1880, ii. 620.)

As a stimulant to the circulation, belladonna has probably not been employed as much as it ought. Dr. Graves, however, commends it especially when the pupil is contracted in *typhus fever*, and it has been used with asserted advantage in *erysipelas*, *scarlet fever*, etc. I think this use of belladonna offers a very inviting field for therapeutic investigation.

To arrest Secretion.—Arresting secretion of the salivary glands by paralyzing the extreme branches of the chorda tympani has already been shown to be a physiological action of belladonna, and it follows from this that the drug should be useful in *ptyalism*. I have tried it in several cases of *mercurial salivation*, and found that it arrests almost at once the discharge of saliva, and seemingly facilitates greatly the return to health. In *colliquative sweats* it was originally recommended by Prof. Da Costa (*Phila. Med. Times*, Feb. 15, 1871), and I have found it of very great service. A full dose of belladonna extract, or one-sixtieth to one-eightieth of a grain of atropia used hypodermically, at bedtime, will very frequently prevent the usual *night-sweat*. In *colliquative diarrhœa* it has been recommended by M. Delpage, and very probably will be found of service.

Inunctions of the breasts with belladonna ointment are habitually employed for the purpose of arresting the secretion of milk, and in the experiments of Hammerbacher upon a goat atropia given internally lessened the secretion, especially of the watery portions of the milk (*Arch. f. Gesammt. Physiolog.*, xxxiii. 228).

Employment in Poisoning.—It is stated that as far back as 1570 it was asserted that opium and belladonna are, in their influence upon the system, antagonistic. In the early part of the present century their employment as counter-poisons was again brought prominently before the profession; but, although a few scattered earlier records of their use as such exist in medical literature, it was not until the paper of Dr. Wm. F. Norris appeared (*American Journal of the Medical Sciences*, Oct. 1862) that general attention was attracted to the subject. Since this publication, very many cases of the use of the one medicine in poisoning by the other have been published. The opposite actions of belladonna and of opium upon the pupils no doubt first suggested the idea of their antagonism; but in the light of recent experiments these apparently opposite effects upon the eye cannot be considered as proving any antagonism between the drugs, since it is almost certain that the dilatation is due to a peripheric and the contraction to a centric influence. In an investigation by Dr. J. Hughes Bennett (*Brit. Med. Journ.*, 1874, 547), twenty-one rabbits received what previous experimentation had shown to be a fatal dose of meconate of morphia (10 grains), and afterwards sulphate of atropia; six recovered; and of these six, four some weeks afterwards were killed by a dose of 10 grains of the morphia salt. Eleven rabbits received a dose of sulphate of atropia (1¾ to 2 grains), and afterwards 10 grains of the meconate of morphia; seven recovered, and some weeks afterwards the meconate of morphia (10 grains) being given, four of them succumbed to it. Again, two dogs received the fatal dose of meconate of morphia (2¼ grains), and afterwards sulphate of atropia, and recovered, only to die some days afterwards from the effects of a second two-and-a-quarter grain dose of the opium salt. These experiments certainly warrant the conclusion of Dr. Bennett that atropia is physiologically antagonistic to morphia within a limited area, and that it exerts in dogs and rabbits a beneficial influence in opium-poisoning. Dr. Corona has experimentally reached conclusions very similar to those of Bennett (*London Med. Record*, 1877, p. 341). What I affirmed in the first edition of this work, namely, that our present knowledge of the physiological action of the two drugs renders anything like complete antagonism very improbable, is still as true as it is obvious.

When the subject in hand is looked at from its clinical aspect, the conclusion of Dr. Bennett is confirmed. To tabulate and discuss the reported cases of opium- or belladonna-poisoning in which the counter-narcotic has been used would require very many pages, and I therefore can only state my opinion that these records establish the therapeutic value of atropia in opium-poisoning; but this does not indicate, much less prove, complete antagonism between the two drugs. No one would question the value of alcohol in certain stages or conditions of opium-poisoning, and yet no one would claim that opium and alcohol are in any sense antagonistic. In opium-poisoning, death occurs chiefly through failure of the respiration. Atropia is the only known drug which exerts a decidedly stimulating effect upon the respiratory centres. It is evident that in advanced stages of opium-poisoning this property renders atropia an invaluable remedy. In protracted opium-narcosis the cardiac and vaso-motor actions of atropia are of service; but it should never be forgotten that the main influence for good is upon the respiratory centres.* The first improvement from atropia in these cases is usually increased frequency of respiration; and as the breathing becomes less embarrassed the other symptoms ameliorate, largely because of the increased aeration of the blood.

The double nature of profound opium-narcosis must not be lost sight of: the blood is saturated with carbonic acid almost to the dead-line, and much of the unconsciousness, much of the failing circulation, much even of the embarrassed respiration, is due to the presence of the gas. As soon as the system is in a measure relieved of this load, it begins to rebound; emetics act, consciousness returns to some extent, the circulation frees itself, and the road leading towards health is entered upon. It is a matter of the gravest practical importance to decide when, how, and in what quantities the mydriatic should be employed. The exhibition of belladonna should, I think, commence so soon as there is decided failure of the respiration. The stomach is so paralyzed in the narcosis that it is uncertain how fast absorption will take place in the viscus; and the drug should always be given hypodermically, in the form of the alkaloid if possible. The first injection of atropia should be of such size that it could not possibly do harm, and one-fortieth of a grain is in most instances a fair commencing dose. Very generally several repetitions of this are necessary, and the delicate practical point is to decide how often these repetitions shall be indulged in.

I think that very frequently too much atropia is given, and believe that often a great deal of firmness is required in these cases not to use it too freely, especially since reliance is generally placed upon the pupils as a guide. They are, however, a very unsafe guide, as is apparent when it is remembered that whilst opium contracts them by influencing the nerve-centres, atropia probably dilates them by acting on the peripheral nerves. It must not be forgotten that in doses of sufficient magnitude atropia paralyzes the nerve-trunks, and may thus increase the danger. A cardinal principle should, therefore, be to give no more of the mydriatic than is absolutely necessary. One-fortieth or one-sixtieth of a grain may be injected every fifteen, twenty, or thirty minutes, as the urgency of the symptoms may demand. The judgment should be formed from a bird's-eye view of the whole case, fresh atropia not being given so long as the respiration and other symptoms are undergoing amelioration, but the dose being renewed so soon as any tendency to a relapse is manifested. Thus, if under the influence of atropia in a case the respirations had risen from four to eight per minute, I would not use the counter-poison again until there was manifested a tendency for the respirations to grow less frequent, or unless for a long period there had been no improvement.

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* In the experiments of Heubach and Auerbach it was found that atropia produced very decided effects upon the circulation and respiration curves of dogs poisoned with opium. See *Berlin. Klin. Wochensch.*, 1878, 767.

Atropia is useful in other poisonings than that of opium. It has been especially commended as an antidote to *poisonous* fungi.*

As a Local Sedative.—Locally and freely applied, belladonna is a sedative; and, I believe, to glandular as well as to muscular and nervous tissues. In this way it is often very useful in various local inflammations. In the form of a plaster it frequently appears to do good in *palpitations* of the *heart.* Its use locally in spasms and neuralgia has been sufficiently dwelt on. In *mastitis*, or when it is desired to dry up the secretion of milk, its local application to the breast is often very efficacious. Whenever belladonna is used locally, in order to get its good effects it must be employed freely. At the same time, it should be remembered that a number of cases of poisoning by its external use have been reported (*Medical Times and Gazette*, Nov. 1856; also *London Pharmaceutical Journal*, 1871). In children it must be used with very great caution; in adults, with a reasonable amount of care, its external use is safe, provided directions be given to have it washed off so soon as any affection of the sight or dryness of the throat is induced.

Having myself no practical knowledge of diseases of the eye, Dr. Wm. F. Norris, Clinical Professor of Diseases of the Eye in the University of Pennsylvania, at my request, has prepared the following section:

The Use of Atropia in Diseases of the Eye.—Pure atropia, from its slight solubility in water, is only applicable where we desire a moderate effect; the sulphate, however, can be dissolved in water in any desired proportion, and, therefore, is generally employed. When a four-grain solution of this salt is dropped into the conjunctival sac of a healthy and emmetropic eye, we find that in about fifteen minutes the pupil commences to dilate, and that this dilatation rapidly increases, till in from twenty-five to thirty-five minutes it has attained its maximum. The power of accommodation, and consequent ability to read fine print, does not show any marked decrease till twenty-five minutes have elapsed, when the near point commences rapidly to recede from the eye, until in an hour and a half to an hour and forty minutes the power of accommodation is completely annulled, and only objects over twenty feet distant from the eye, or those presenting practically parallel rays, can be distinctly seen. On the second day after the application the power of accommodation begins to return, and increases rapidly up to the sixth day, but is usually not fully regained till from ten to fourteen days; the pupil remains with but little change till the third day, when it rapidly contracts, but has not fully regained its normal state till eleven or twelve days have elapsed.* The mydriatic action of the drug is far more marked from a moderately strong solution applied to the conjunctiva than from its internal use, even when it has been pushed to the production of symptoms of poisoning. Thus applied, it acts on the intraocular nerves and ganglia; and it has been proved by Graefe and Donders that when the aqueous humor of an animal is drawn off and collected after its application, it contains a sufficient amount of the drug to cause dilatation of the eye of another animal when applied to it. These experiments have been abundantly confirmed by later observers, and the rapidity of its action appears to depend on the thickness of the cornea and the age of the subject selected for the experiment. It will be apparent from the foregoing statements that the use of a strong solution of atropia is not to be undertaken without due consideration, inasmuch as it is likely to debar the patient from any satisfactory use of the eyes for a period of from five to ten days. It is, however, invaluable, from its annihilation of the accommodation, where we wish to determine with accuracy the refraction of the eye, and is daily used for this purpose in cases of hypermetropia where the patients find it impossible to relax their accommodation, in astigmatism where it is necessary to determine the exact difference between the two principal meridians of the cornea, and in the rare cases of myopia associated with spasm of the ciliary muscle. To obtain this complete paralysis of the accommodation, a few drops of a four-grain solution should be dropped in the eye, and this repeated after an interval of five minutes. The patient will be ready for examination one and a half hours subsequently. In the vast majority of cases it is entirely unnecessary to dilate the pupil to obtain a satisfactory view of the fundus with the ophthalmoscope; but where this becomes necessary we can often use with advantage a solution of one-twentieth grain in an ounce of water; a drop or two of this will dilate the pupil, without, however, rendering it absolutely immovable, and with scarcely any interference with the accommodation; on the next day the pupil is much smaller, and on the third day no trace of its action remains. In cases of suspected cataract the pupil should always be dilated; otherwise we may readily fail to discover the lesion, which frequently first manifests itself in a few faint striæ shooting out from the periphery of the lens. Moreover, it affords us a valuable prognostic point as to the probable success of any operation where the cataract is ripe; for where the iris fails to dilate ad maximum, we may be sure that it is more prone to take on inflammatory action, and more liable to be pressed on by any cortical matter which may remain behind in the eye. Daily experience shows that after the evacuation of the aqueous humor in the operation for cataract, the iris will contract in spite of any previous use of atropia; but as soon as by the closing of the wound the humor reaccumulates and the anterior chamber is re-established, the atropia resumes its sway. It is most useful in all inflammations of the cornea. In *phylctenular keratitis*, by its local anæsthetic action on the branches of the trigeminus, it diminishes the photophobia and blepharospasm, and seems to mitigate the intensity of the inflammation by its influence in contracting the ciliary vessels, thus diminishing the supply of nutritive material carried to the cornea. Where an ulcer has perforated the central region of the cornea, and a prolapse of the iris has ensued, the energetic use of atropia often enables the radiating fibres of the iris to detach it from the cornea as soon as the opening has been plugged by lymph, and the anterior chamber restored, thus preventing the formation of anterior synechiæ. Mackenzie long ago called attention to the "healing and anodyne" effect of atropia in ulcers of the cornea occurring in the ophthalmia of new-born children,—a fact since universally recognized, and which holds good equally in the ulcers resulting from other forms of purulent conjunctivitis. It is held by many writers that part at least of this beneficial action is to be ascribed to its diminution of intraocular tension.* In cases of *iritis* a strong solution of atropia should at the outset be applied repeatedly at short intervals until we have obtained a full dilatation of the pupil, and subsequently sufficiently often to maintain the iris in this condition. We thus place the inflamed tissue at rest, diminish its blood-supply, and prevent the formation of posterior synechiæ, which constitute so frequent a cause of the recurrence of this disease by their mechanically-irritating effect: putting a strain on the iris in its every motion, hindering that variation in the diameter of the pupil which normally takes place with every change of convergence and with every variation of the intensity of light. Moreover, extensive synechiæ where the iris is plastered down to the anterior capsule by large patches of lymph tend to produce cataract, by interfering with the nutrition of the lens. Where the synechiæ are narrow and tongue-shaped, they may often be torn through by its action, even after the lapse of years.

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* Consult *The Doctor*, 1874; *Brit. Med. Journ.*, ii. 1874; *Arch. Physiol. Normale*, 1877, p. 831.

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* For a more detailed discussion of this subject, see *Donders's Anomalies of Refraction and Accommodation*, p. 584, New Sydenham Society, 1864.

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* That atropia diminishes intraocular pressure has been asserted by Graefe, Coccius, and many good authorities; and a reference to any manual of diseases of the eye will show that it is an accepted doctrine with most clinical observers of the present day. Other weighty authorities, such as Donders and Stellwag, doubt its ability to produce any such effect. Certainly it fails to reduce intraocular pressure in cases of glaucoma. Numerous attempts to decide the question by physiological experiment have been made by Hensen and Völckers, Wegner, Adamiuk, Grünhagen, Dor, etc. The results vary, however, considerably among themselves. Those with the manometer are open to the objection that the cutting open the eyeball for its introduction quite changes the conditions of intraocular pressure and circulation, and that very slight movement of the instrument or eyeball invalidates the results; while those with the tenometer are also unsatisfactory, inasmuch as we have yet failed to obtain any reliable instrument for measuring intraocular tension.

Atropia acts more powerfully in iritis after the abstraction of blood,[*] and occasionally, where there is much exudation, fails to produce its effect till after the constitutional effect of mercury has been obtained. In some individuals the instillation of a strong solution of atropia, by its rapid passage through the tear-passages into the nose and throat, produces symptoms of slight belladonna-poisoning,—viz., flushed face, rapid pulse, dryness of the throat, slight dysphagia; but this may usually be diminished or prevented by gargling the throat with water, by compressing the canaliculi, or by everting the lower punctum lachrymarum. In some individuals it produces a curiously-irritant action on the conjunctiva, known as atropine conjunctivitis; this is sometimes quite severe, calling forth almost erysipelatous symptoms, at other times bringing out a crop of granulations. This is owing to idiosyncrasy, and will then happen with perfectly neutral solutions. It should in such cases be discontinued, and the conjunctivitis which it has called forth combated by weak solutions of alum and sulphate of zinc or other mild astringent. We find, too, in some cases of iritis, especially those occurring in rheumatic patients with posterior synechiæ due to repeated previous attacks, that we not only fail to dilate the pupil, but that atropia acts as an irritant to the eye. We are then obliged to give up its use, and resort to the application of dry warmth and appropriate constitutional remedies. Atropia will occasionally, in cases of chronic glaucoma, precipitate an acute attack, and is, therefore, to be used with due consideration in this disease.[†]

A great deal has been written about the value of belladonna as a prophylactic in *scarlatina*, and authorities differ very much. For a discussion of the subject I must refer the reader to the treatises of Dr. Geo. B. Wood, of Dr. Stillé, of Dr. Waring, etc. I have never had a decisive opportunity of testing the matter, but have no faith in the efficacy of the remedy. It ought to be tried further, however. The plan practiced has been to dissolve two grains of the extract in a fluidounce of water, and give two drops daily to a child a year old, adding one drop for every year in older children up to twelve years.

TOXICOLOGY.—Sufficient has already been said about the general symptoms of belladonna-poisoning. Those which are characteristic are the dryness of the throat, the increased frequency of breathing, the dilated pupils, the red efflorescence on the skin, the rapid pulse, the active talkative delirium, sometimes convulsions, all ending in abolition of function, as shown by stupor, rapid feeble pulse, cold extremities, and paralysis. If the urine of a patient suffering from belladonna-poisoning be dropped into the eye of the cat or rabbit, it will dilate the pupil; and the diagnostician may avail himself of this test in any doubtful case. Dr. Morel (*Annales de la Société de Médecine de Gand*, 1873) calls attention to a sort of laryngitis produced by poisonous doses of belladonna, and characterized by pain in the larynx, roughness of voice, and the expectoration of minute, pearly, tough pellets. It was present in the advanced stages of two cases of poisoning under his care.

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[*] Mackenzie, *Diseases of the Eye*, p. 537, London, 1854. Graefe, *Archiv für Ophthalmologie*, vol. ii. part 2, p. 209 (note).

[†] Graefe, *Archiv für Ophthalmologie*, vol. xiv. 2. 117. H. Derby, *Trans. Amer. Ophthal Soc.*, p 35, 1868. Wells, *Diseases of the Eye*, p. 517 (2d Amer. ed.).

The minimum fatal doses of the preparations of belladonna are scarcely known. An enema representing eighty grains of the root has produced death in five hours (*Casper's Wochenschrift*, Feb. 1845); but, on the other hand. recovery has occurred after the ingestion of three drachms of the extract (Taylor's *Principles and Practice of Medical Jurisprudence*, London, 1873, p. 432). A tenth, or even a twentieth, of a grain of atropia will often produce alarming symptoms; yet Dr. Chambers reports (*Lancet*, 1864) recovery in a child four years old who had taken about two teaspoonfuls of a solution containing a grain of the alkaloid in half an ounce.

After death from belladonna, no characteristic lesions are to be found.

In the treatment of belladonna-poisoning, the first indication is to prevent the absorption of any more of the poison. For this purpose emetics or the stomach-pump should be used. The same difficulties are to be met and the same measures adopted as in opium-narcosis; and, as in opium-poisoning it is well to exhibit tannic acid freely, because it forms with the alkaloids salts which are soluble with difficulty, so should vegetable astringents be given when an overdose of belladonna has been ingested. After the stomach has been evacuated, symptoms must be met as they arise. During the first febrile stage I would not hesitate to use cold bathings; and the moderate use of tartar emetic, or other sedative, is perhaps justifiable. The value of opium in belladonna-poisoning has not, I think, been determined, and its use should only be tentative, although good is to be expected from its judicious employment. In poisoning by a mydriatic, in order to keep up the respiration and the circulation during the stage of failure of function the same measures should be employed as in opium-poisoning. External stimulation by heat and by mustard, flagellations, etc., artificial respiration, and especially the use of the alternate cold and hot douche, should all be practiced as necessary. Physostigma and jaborandi appear to be somewhat antagonistic to atropia within certain limits, and jaborandi has been used in atropia-poisoning (*Lancet*, 1876, i., p. 346). As this subject can best be elucidated after the discussion of the action of the respective drugs, the reader is referred for further information to the articles upon Calabar bean and jaborandi. After toxic doses of belladonna, there is very generally complete retention of urine; and as this secretion contains the greater part of the ingested poison, and as reabsorption in the bladder is at least conceivable, the catheter should be used early.

ADMINISTRATION.—Belladonna is never used internally in substance. All the preparations of the U. S. Pharmacopœia except two (designated below) are made from the leaves. They are the *tincture* (*Tinctura Belladonnæ*—1 to 6.66, U.S.), dose, ten to thirty drops; the *alcoholic extract* (*Extractum Belladonnæ Alcoholicum*), dose, one-eighth to one-half a grain; the *fluid extract* of the *root* (*Extractum Belladonnæ Fluidum*), dose, one to two minims; the *plaster* (*Empl. Belladonnæ*[*]), represents its weight of root; the *ointment* (*Unguentum Belladonnæ*) contains one-tenth of extract. The *abstract* (*Abstractum Belladonnæ*) represents twice its weight of root, dose, one grain. The *sulphate of atropine* (*Atropinæ Sulphas*) is most commonly used, on account of its solubility in water. One-sixtieth of a grain of atropia or its salt, given hypodermically, will generally produce slight dryness of the throat or other indications of its constitutional action. Where rapidity of action is required, this is the best method of administering belladonna.

Hydrobromate of Homatropine.—Homatropine is an alkaloid artificially produced from atropia, the hydrobromate of which is preferred for practical use on account of its being stable and not hygroscopic. It is said to produce, when taken internally, symptoms similar to those caused by atropia, except that it slows the pulse,—an observation which needs confirmation. Dr. Wm. MacIntosh (*Unpublished Inaug. Diss.*, University of Pennsylvania, 1883) has found that, like atropia, it causes in the frog first paralysis with abolition of reflex action, followed, if the dose has not been too large, by tetanus: in the first period the conducting power of the motor nerves was much depressed: tying an artery was found to prevent the development of paralysis in the protected leg: the pneumogastrics were peripherally paralyzed. If a solution of the alkaloid (gr. iv–f℥i) be put in the eye, the pupil usually begins to dilate in fifteen minutes, and the effect passes off in as many hours. As a paralyzer of accommodation the salt is too feeble for advantageous use; but when it is desired merely to examine the fundus oculi, the fugaciousness of its action makes it a valuable mydriatic.

STRAMONII FOLIA—STRAMONIUM LEAVES. U.S.

STRAMONII SEMEN—STRAMONIUM SEED. U.S.

The leaves and seeds respectively of the Datura Stramonium, or *Jamestown Weed*, a coarse, bushy, annual herb, three or four feet high, growing in waste places both in this country and in Great Britain, and readily distinguished by its large, funnel-shaped, whitish, fetid flowers, and its quadrivalve spinescent capsules. The leaves are large, smooth, ovate, irregularly sinuate, with large acute teeth. The seeds are small, brownish-black, reniform, with a feebly-bitterish narcotic taste. The active principle is an alkaloid discovered by Geiger and Hesse, and named *Daturine*, but which, according to Ladenburg, is a mixture of atropine and hyoscyamine.

Physiological Action.—The physiological evidence as to the identity of *daturia* and *atropia* is in strict accord with the chemical proof. The symptoms of poisoning by stramonium differ in no respect from those of belladonna-poisoning, although Laurent (*De l'Hyoscyamine et de la Daturine*, Thèse, Paris, p. 22, 1870) asserts that irregularity of the heart's action is more marked under the influence of stramonium. The same accelerated pulse, the same elevation of temperature, the same wild delirium, the same increased frequency of respiration, the same widely-dilated pupils, the same red efflorescence on the skin, the same restlessness or convulsions, occur in both cases, and, when the dose has been sufficiently large, end alike in abolition of the functions of circulation, respiration, and innervation: stupor, general paralysis, weak, rapid, thready pulse, threatened asphyxia, constituting the phenomena of the closing scene in poisoning from either narcotic.

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[*] Constitutional symptoms are readily produced by the free external use of belladonna plaster or ointment; and patients should always be warned to remove the plaster if dryness of throat or disorder of vision come on. For cases of poisoning in this way, see *N. Y. Med. Record*, Jan. 1884, also *Journ. Amer. Med. Assoc.*, ii. 122.

The most careful minute investigation of the physiological action of daturia which I have met with is that of Charles Laurent, already quoted. In his experiments that observer found that under the microscope the capillaries of the frog's web could be seen to contract after the application of daturia, even when the nerves of the limb had been previously severed, and after the hypodermic injection of the alkaloid; that the pulse-rate and arterial tension were both augmented by small doses of the poison, but that by large doses the arterial tension was diminished, although the pulse was still increased in frequency; that when the heart was completely separated from all connection with the central nervous system, daturia reduced the number of its beats; that respiration is accelerated by the alkaloid, even after section of the pneumogastrics; that by moderate doses of the alkaloid the conducting power neither of the sensory nor of the motor nerves is destroyed; that the muscular contractility is not affected; that small doses increase, large ones diminish, intestinal peristalsis. Elaborate discussion of these facts seems unnecessary. It is seemingly demonstrated, from both a chemical and a physiological point of view, that *daturia* and *atropia* are identical.

THERAPEUTICS.—Stramonium may be used to meet precisely the same indications as belladonna. It has been especially employed in spasmodic *asthma*, chiefly in the form of cigarettes made by rolling up the dried leaves. These are often very efficient when there is no organic disease; but their use requires some caution, as very alarming symptoms, if not fatal results, have been produced by them. In the form of cataplasms, stramonium leaves are often applied with advantage to painful *local inflammations*, *inflamed hemorrhoids*, etc.

ADMINISTRATION.—The officinal preparations of stramonium are all made from the seeds. They are the *extract* (*Extractum Stramonii*, U. S.), dose, one-fourth to one-half a grain; the *tincture* (*Tinctura Stramonii*—1 to 10, U. S.), dose, ten to twenty minims; and the *fluid extract* (*Extractum Stramonii Fluidum*, U. S.), dose, one to two minims.

TOXICOLOGY.—Accidental poisoning, especially of children, by stramo-

nium, is very common. In all points, as regards both symptoms and treatment, stramonium- and belladonna-poisoning are alike.

HYOSCYAMI FOLIA—HYOSCYAMUS LEAVES. U.S.

Hyoscyamus niger is a coarse herbaceous biennial, indigenous in England, and naturalized in the Northern United States. The leaves, which alone are officinal, are large, oblong-ovate, deeply sinuated, and very hairy. In 1821 Peschier announced the existence of an alkaloid in hyoscyamus, but it was not until 1833 that Geiger and Hesse succeeded in obtaining it pure. According to Geiger, when slowly crystallized, *Hyoscyamia* occurs in transparent needles, and in star-shaped or bushy clusters of crystals. According to the recent researches of Ladenburg, hyoscyamus contains two alkaloids: one is crystallizable, has the same chemical formula as atropine, and constitutes the *crystalline hyoscyamine* of commerce, and its *sulphate* is the *Hyoscyaminæ Sulphas* of the U. S. Pharmacopœia; the other is amorphous, constitutes the *amorphous hyoscyamine* of commerce, and, although having the same chemical formula as hyoscyamine, is diverse from it; to it Ladenburg gives the name of *hyoscine*.

Physiological Action.—Hyoscyamia has a very similar, if not identical, action with atropia. Schroff* asserts that it is decidedly more powerful than atropia, so far at least as concerns its local action on the pupil. On the other hand, Lemattre (*Archives Générales*, 1865) has found atropia much the more active of the two. It is, however, scarcely doubtful that the latter observer had an impure hyoscyamia, and it seems to me that it cannot be at present considered as determined that there is any marked difference in the mydriatic activity of the two drugs. Both Schroff and Düllenberg have noticed in man, as the result of the ingestion of hyoscyamus, dryness of the throat and mouth, brief sinking of the pulse-rate, followed by increased frequency, mydriasis, giddiness, muscular weakness, and insecurity of gait. The experiments of Schroff, of Laurent, and especially of Harley (*The Old Vegetable Neurotics*), indicate that hyoscyamus is much more of a hypnotic than is belladonna. Yet Harley's recorded observations would seem to show that, in some individuals, hyoscyamus induces insomnia. According to Harley, the primary sinking of the pulse is much more marked after hyoscyamus than after its sister-narcotic. Laurent (*De l'Hyoscyamine et de la Daturine*, p. 15) affirms that the delirium caused by hyoscyamus is calm, whilst that by atropia is furious; but on page 19 of his book is recorded a case of henbane-poisoning in which the delirium was "furious." Schroff (*Wochenblatt der Zeitschrift der Gesellsch. der Aerzte zu Wien*, 1865) asserted that pneumonia is a constant and even characteristic lesion of hyoscyamus-poisoning in the rabbit; but Lemattre (*loc. cit.*) has never seen more than little scat-

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* Quoted by Husemann, *Die Pflanzenstoffe*, p. 474.

tered points of hyperæmia ;. and in Laurent's experience even these have always been absent.

In the elaborate research of Laurent it was found that the capillaries of the frog's web contracted after the local application of hyoscyamia, even when the nerves had been previously severed, and also after the hypodermic use of the poison; that small doses augmented both the pulse-rate and the arterial tension, whilst large doses increased the former and diminished the latter; that the direct application of the alkaloid to the heart produced a rapid diminution of the number of its beats; that moderate doses increased the rapidity of respiration even after section of the pneumogastrics; that upon the nervous system, the muscles, and the intestines, the action of hyoscyamia was the same as that of daturia. The more important of these conclusions were also experimentally arrived at by Heilman (*Beiträge zur Kenntniss der physiol. Wirkungen des Hyoscyamins*, etc., Jena, 1873). Dr. R. Gnauck found (*Verhandl. d. Physiolog. Gesellsch. zu Berlin*, Aug. 1881) that hyoscyamine agrees with atropia in its action upon the vagus and heart-muscle, but is less powerful and persistent in its influence, and also acts as a powerful soporific: it further appeared especially to dilate the internal abdominal vessels.

THERAPEUTICS.—Hyoscyamus may be used to fulfil any of the indications for which belladonna is employed. Clinical experience appears in a measure to bear out the assertions of various authorities as to the superiority of hyoscyamus as a hypnotic. It has been much employed by alienists in various forms of delirious insanity (*West Riding Lun. Asyl. Med. Reports*, v.; *London Practitioner*, xvii. p. 17; xx. p. 85; *Lancet*, 1879, ii.; *Archives of Med.*, 1880). Many of them claim that hyoscyamia has a very especial calmative effect. The diagnosis and treatment of the poisoning are identical with those of belladonna.

The preparations are the *alcoholic extract* (*Extractum Hyoscyami Alcoholicum*, U. S.,—dried leaves), dose, one to three grains, and the *tincture* (*Tinctura Hyoscyami*—dried leaves 1 to 6.66, U.S.), dose, half a fluidrachm to two fluidrachms.

Before we can reach positive results with hyoscyamus it is necessary that the *isolated* crystallized *alkaloids* be separately studied. Dr. J. C. Shaw (*Journ. Nerv. and Ment. Dis.*, vii. p. 27) has recently partially studied crystallized and presumably pure *hyoscyamia*, and found that it affects the system of voluntary movement and the circulation, including the heart, and the vaso-motor system exactly as atropia does. In a single experiment the respiration did not seem to be affected as by atropia; but this is contradicted by results arrived at by previous experimenters, and needs confirmation. Upon man Dr. Shaw believes, as do many alienists, that hyoscyamia acts as a soporific. He also states that it is less powerful as a mydriatic than atropia, and diminishes the respiratory rate. It must be remembered that these studies have been made upon lunatics; before the conclusions can be accepted as established, much more elaborate experimental researches are necessary, also studies upon normal individuals, and especially contrasting studies made with atropia and hyoscyamia upon maniacs; by the use of alternate doses upon the same individual any difference of action of the two drugs could readily be detected. It should also be remembered that in his studies upon normal men Dr. Richter noted no tendency to sleep (*Neurologische Centralb.*, i. 294).

In a careful comparative study of hyoscyamia and atropia upon a case of acute mania by Prof. Sydney Ringer, the two alkaloids were found to act practically alike (*London Practitioner*, March, 1877). Commercial *hyoscyamia* was formerly very impure, and a grain has been given with impunity; but one-fortieth of a grain of the pure alkaloid has produced violent poisoning (*Lancet*, 1879, i. 474).

I have made recently (*Therapeutic Gazette*, Jan. 1885) a careful study of *hyoscine*, both upon man and upon animals. In the frog it produces a general motor and reflex paralysis, progressively increasing until death from failure of respiration. When recovery occurs, there is no stage of tetanus following the palsy. Neither the muscle nor motor nerves are sensibly affected, and the paralysis is dependent upon depression of the motor centres of the spinal cord. No evidence could be obtained of affection of the sensory side of the nervous system. In mammals, the symptoms produced are loss of muscular power, disturbance of respiration, and marked tendency to stupor, and finally death by asphyxia. The alkaloid has very little effect upon the circulation, though after enormous doses when life is maintained by artificial respiration the vaso-motor system is finally paralyzed. On the heart itself hyoscine acts as a very feeble depressant; it does not paralyze the pneumogastrics. In man the symptoms which are produced by decided doses are dryness of the mouth, flushing of the face, great sleepiness, associated in some cases with semi-delirious mutterings, and a feeling of giddiness like that of intoxication. The respirations are usually lessened in frequency, and the pulse-rate is also somewhat diminished; mydriasis is sometimes produced, but does not always follow even large doses. In the case of Dr. H. A. Hutchinson (*Alienist and Neurologist*, iii., p. 539), who took a quarter of a grain of very impure hyoscine, quiet coma with entire muscular relaxation was produced, and lasted eleven hours. It is evident that in man as in animals the motor tract of the spinal cord and the cerebral cortex are especially affected by this alkaloid, which is also a respiratory paralyzant. I have used it as a therapeutic agent in a number of cases of delirious excitement occurring in insane persons, with, in most cases, remarkable effect in producing sleep, often after the failure of chloral and morphia. In delirium tremens it has sometimes seemed of great service, in other cases failed. It has been used by Prof. Edlessen (*Centralb. f. Med. Wissensch.*, 1881, 416) with asserted good results in *asthma*, and also in *whooping-cough*. Dr. Rudolph Gnauck (*Centralb. f. Med. Wissens.*, 1881, 801; *Charité Annallen*, 1882, 448) also affirms that hyoscine has a very powerful hypnotic influence, and tends to reduce the pulse-rate. He has found that in some cases it causes general distress, headache, numbness, etc. In one or two of my own cases it seemed to disagree with the patient, but usually there have been no after-effects, or other unpleasant symptoms. In the therapeutic dose the drug is tasteless, and it may be administered to insane patients in their food or drink without their knowledge. In my own experience it has failed entirely in the relief of pain. But in *sleeplessness* from cerebral excitement it will probably prove one of our most useful remedies. It is free from irritant properties and may be used hypodermically, either in the form of the *hydriodate* or *hydrobromate*, which salts occur in crystalline form in commerce, and are soluble. The only reliable preparations at present upon the American market are those of Merck, of Darmstadt; the dose is hypodermically 1–100 of a grain, by the mouth, 1–60 to 1–90 of a grain. The influence of the single dose seems to last from six to eight hours.

CLASS VIII.—ANÆSTHETICS.

THE term *Anæsthetics* is here employed as the name of a group of volatile substances, whose vapor has the power of producing loss of consciousness, preceded by or accompanied with loss of sensibility and diminished muscular action. The medicinal properties of these substances are largely due to their volatility, by virtue of which they are very rapidly absorbed and almost as rapidly eliminated by the mucous membrane of the lungs. As a consequence of this, their action is very easily controlled. That they are taken into the blood, and thereby reach all portions of the system, has been abundantly proven by recent investigations.*

The action of the anæsthetics certainly is upon the nerve-centres. Thus, Bernard has shown (*loc. cit.*) that a ligature so placed as to cut off all circulation from the posterior part of the frog does not prevent the production of abolition of sensation, voluntary motion, and reflex action in the hind legs when an anæsthetic is injected into the anterior part of the body.

Many of the theories which have been suggested to explain the production of anæsthesia are so groundless that it seems unnecessary to discuss them here. All that are worthy of consideration may, I think, be arranged in four groups, as follows: 1st, those which assert that the symptoms are produced by a partial arrest of oxidation; 2d, those which look upon anæsthesia as due to precedent physical changes in the blood; 3d, those which assert that anæsthesia, like sleep, is due to cerebral anæmia; 4th, those which teach that the various agents employed act directly upon the various organs and tissues concerned,—including in this group the recently-propounded theory of Bernard that anæsthesia is produced by a semi-coagulation of the nervous protoplasm.†

As the theories of the last group are the most natural, the burden of proof rests upon the supporters of the other theories. All the proofs of the first two groups as yet brought forward amount to no more than as follows: that in asphyxia the symptoms are similar to those of anæsthesia; that in profound anæsthesia there is an evident lessening of oxidation; and that some anæsthetics probably produce changes in the blood.

The objections to regarding these facts as proving the truth of the theories alluded to are very grave. Thus, it is very well ascertained that the symptoms of asphyxia are only analogous to those of anæsthesia, not identical,* and indeed that anæsthesia as caused by different agents offers different phenomena; also, there is no proof whatever that the lessened oxidation and the blood-changes which are believed to occur when anæsthetics are employed are causes of the nervous symptoms, and not simply coincident phenomena. It must be insisted on, therefore, that these theories have never been proven. Moreover, positive proof of their incorrectness is not wanting. Thus, in regard to the theory of arrest of oxidation, there are substances, such as nitrite of amyl, which lessen oxidation very remarkably (Richardson, *Medical Times and Gazette*, p. 180, 1868), but are not anæsthetics; and an excess of oxygen in the air does not lessen the rapidity with which anæsthesia is induced.† The Anæsthetics Committee of the British Med. Association (*Jour. Anat. and Phys.*, xiii. 224) also found that during chloroform narcosis there was an actual increase in the elimination of carbonic acid. In regard to the blood-theories, Ludimar Hermann (*Reichert's Archiv für Anatomie*, 1866, p. 27) calls attention to the fact that the anæsthetics produce the same general symptoms in the infusoria, which have no red blood, as in mammals; and Lewisson‡ has shown that they influence the so-called "salt frogs," which contain little or no blood, precisely as they do the normal frog, from which the conclusion is inevitable that they do not affect the frog by altering the nature of the blood or by inducing asphyxia, In regard to cerebral anæmia, it appears to be established that it occurs in sleep; and recently Claude Bernard (*loc. cit.*, p. 122) has shown that during the period of excitement preceding anæsthesia there is cerebral congestion, but during the anæsthesia cerebral anæmia. Cessation of function normally results in anæmia of the organ, and the anæmia of sleep and anæsthesia is, in all probability, an effect, not a cause, of suspended cerebration. In the frog it has been abundantly proven that absolute anæmia of the nerve-centres does not suspend their functions, and that on the bloodless cerebrum chloroform exerts its usual influence. The only theory at all compatible with our present knowledge is that anæsthesia is in most cases due to a direct action, upon the cortex cerebri and other nerve-centres, of the agent inducing it.

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* See especially O. Schmiedeberg, *Inaugural Dissertation*, Dorpat, 1867, *Archiv d. Heilkunde*, viii., 1867; Claude Bernard, *Leçons sur les Anesthésiques*, Paris, 1875.

† For study of the coagulation theory, see *Centralblatt Med. Wiss.*, 1877, p. 609.

The action of the anæsthetic upon the nerve-structure is probably a purely vital one. But by no means all authorities acknowledge this. Many, if not all, of the anæsthetics have the power of dissolving the red corpuscles: and Ludimar Hermann (*Reichert's Archiv für Anatomie*, 1866) has pointed out a possible connection between this and anæsthesia. He states that *protagon*, which constitutes the stroma of the red blood-disks, is an important constituent of the nerve-centres. As death would necessarily occur before the protagon could be dissolved out of the nerve-centres,—*i.e.*, before it could be dissolved out of the red corpuscles,—it is evident that no extensive destruction of the latter bodies can occur from the action of an anæsthetic and the patient survive. Bile-acids also dissolve protagon, and Hermann states that some experiments he has made seem to indicate that they have anæsthetic properties. Before, however, the ingenious theory of Hermann can be considered proven, further investigations must be made. The recent coagulation theory of Bernard rests almost solely upon the asserted but doubtful fact that anæsthetics applied in sufficient concentration coagulate albuminous substances, and appears to me such a pure assumption that its discussion at length is beyond the plan of the present work.

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* See Report of Chloroform Committee, *Medico-Chirurg. Trans.*, vol. xlviii. p. 329.

† Ibid., p. 335.

‡ See *Chloral* for further details.

In 1848 (*Archives Générales*, 2e sér., t. xvi., 1848), Duméril and Demarquay showed that during anæsthesia there is a reduction of temperature. This has been confirmed by Bouisson (*Traité théorique et pratique de la Méthode anesthésique*, Paris, 1850) and by Sulzynski (*Ueber die des Alkohols, Chloroforms und Aethers Einfluss auf den thierischen Organismus*, Inaug. Dissertation, Dorpat, 1865); and Scheinson (*Archiv des Heilkundes*, 1869) has demonstrated that there is no increase in the giving out of heat by the body during anæsthesia, and consequently that the anæsthetics lessen the production of animal heat, no doubt, like alcohol, by checking tissue-metamorphosis.

The action of anæsthetics may be modified by the injection of narcotics. Morphia given hypodermically about half an hour before the exhibition of the anæsthetic is said to have a decided effect in prolonging the anæsthesia. Chloral administered shortly before etherization certainly causes the first stages of the latter to be much quieter than usual, and also prolongs the narcosis.*

The chief purposes for which anæsthetics are used are to *relieve pain* and to *relax spasm*. To meet the first indication they are employed by surgeons especially; but they are also exceedingly valuable in cases of suffering from disease. It must be borne in mind that their action is very transitory, and is accompanied by more or less disturbance of the general system, and that consequently they are to be employed only when the pain is exceedingly severe and transient. To relieve pain, anæsthetics are used with great propriety during *child-birth*.† In natural labor it is not commonly necessary to produce complete anæsthesia. When the full effect of either ether or chloroform is induced, there is almost always a weakening, and very often an abolition, of the uterine contractions. The anæsthetic should be administered in such quantities as to relieve the pain without decidedly interfering with the muscular spasm. In some cases this can be done, in others it is impracticable. I have obtained very advantageous results in some cases by suspending the pains for about half an hour by means of ether, and then entirely withdrawing the anæsthetic. By this treatment the weak, painful, ineffectual efforts of a worn-out nervous patient may often be converted into regular, successful pains. I think that the risk of *post-partum hemorrhage* is materially increased by anæsthetics, and therefore habitually give after their use two drachms of the fluid extract of ergot, as soon as the perineum is well distended by the child's head. Anæsthetics are frequently used in surgery for the purpose of relaxing spasm, as in cases of *dislocation*, *hernia*, etc. In medicine, they have been employed in various forms of *convulsions*, and are especially valuable in severe *hysterical convulsions*, in *puerperal eclampsia*, and in *spinal convulsions;* in *epilepsy*, they are very rarely called for; in *infantile convulsions*, they may be sparingly used when the convulsion itself threatens life. In various *spasms* of *excretory ducts* or *canals*, and especially during the passage of *calculi*, they act very favorably, both by relieving pain and by producing relaxation. In *asthma*, and in *spasmodic stricture* of the *œsophagus*, as in all other cases of oft-repeated spasm, they should be administered only to meet temporary indications, as their habitual use is deleterious.

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* Mr. Bonwill has proposed rapid breathing as a means of producing slight anæsthesia in cases of minor surgery. The patient is required to breathe very rapidly for from three to five minutes, when a condition of partial loss of consciousness, probably dependent upon disturbance of the cerebral circulation, is induced. (See *Phila. Med. Times*, vi., p. 265.)

† I see no reason for believing that anæsthesia of the mother seriously influences the child, and do not think much weight can be attached to the assertions of Dr. Hofmeier (*Berlin. Klin. Wochensch.*, 1883, xx. 230), that there is produced an increased elimination of nitrogen in the new-born babe.

NITROGEN MONOXIDE—NITROUS OXIDE. (NO—N_2O.)

Nitrous oxide is a colorless, almost inodorous gas, of a sweetish taste. It is a very active supporter of combustion. Water absorbs nearly its own bulk of it. It is made by the distillation of the nitrate of ammonium, which resolves itself into the gas and water. Thus, $NO_3NH_4 = N_2O + 2H_2O$. The wood-cut on the opposite page represents the best apparatus,* and the rules appended thereto embody all the necessary instructions for the production of the gas. As they are very concise, they should be followed to the letter.

The various effects of increasing heat upon nitrate of ammonia are: At 226° F. it fuses perfectly; at 302° F. it emits white fumes, condensing in drops; at 347° F. it effervesces slightly; at 356° F. it boils without decomposition; at 437° F. it effervesces rapidly; at 460° F. it begins to evolve gas; at 482° F. it evolves gas in abundance; above 500° F. *nitric oxide* is given off.

To determine the temperature, thermometers have been prepared which may be passed through the cork and into the retort, marking the following degrees: 226°, 356°, 460°, 482°, 500° F.

To obtain the largest amount of gas, the nitrate should first be melted in the retort at a temperature just sufficient (226° to 250° F.). When melted, the heat may be at once carried up to the point of decomposition, 460° F. If a gradually-increasing heat is used after the salt is melted, a portion of it will sublime unchanged until the temperature reaches 460° F. The heat should never be allowed to rise above 482° F., for beyond that noxious products are generated. After the gas has begun to come over briskly, the appearance of copious white fumes in the retort is an indication that the heat is too great. The nearer the heat can be kept at the point necessary to generate nitrous oxide, the purer will be the gas.—Dr. Jas. W. White, *Dental Materia Medica*, Philadelphia, 1868.

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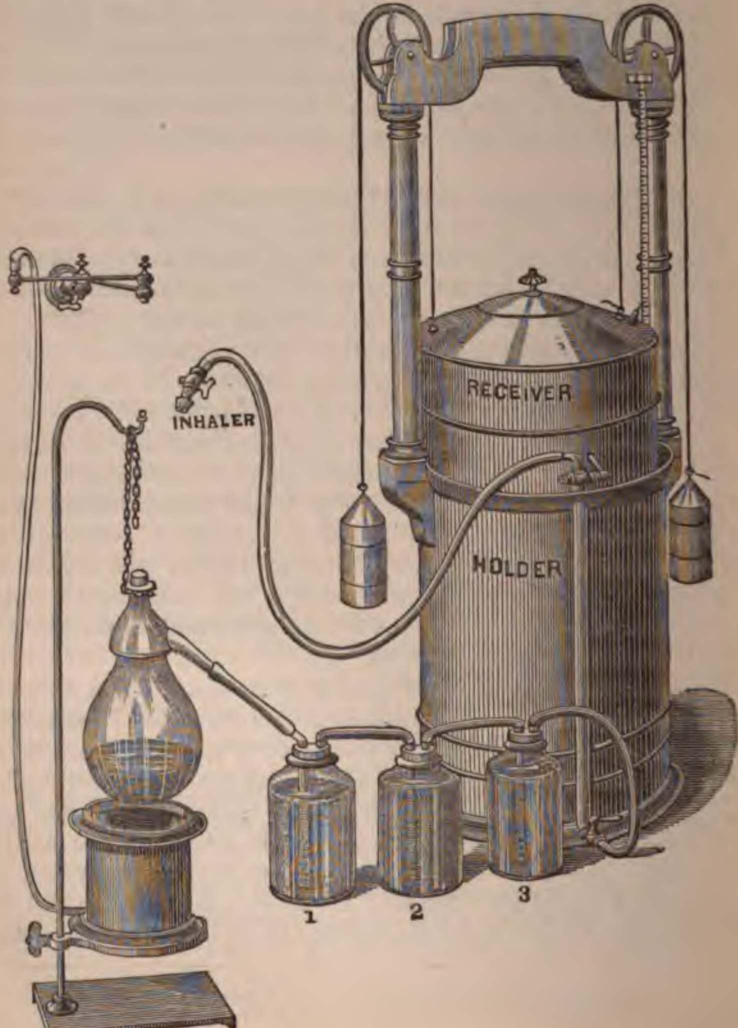
* This apparatus is furnished by Mr. S. S. White, of Philadelphia.

After the gas has commenced to come over freely, it is generally best to lessen the amount of heat applied to the sand-bath. The gas should be allowed to stand over water for a few hours before using. It improves rather than deteriorates by age, and in a properly-constructed gasometer may be kept for many weeks, especially if the water between the holder and receiver of the gasometer be covered with a thin film of oil, so as to prevent its yielding to the air the gas which it absorbs, until saturated. In manufacturing the gas, whenever the alkalinity of the potash solution in the jar No. 2 is lessened, all the washing-jars should be emptied and refilled.



Place the holder in a level position, and fill it with water to within an inch or two of the lower edge of the taper rim. Open all the spigots, especially the one in the top of the receiver, and gently sink it into the water; then close the spigot in the top of the receiver and that on the upper edge of the holder, and arrange the weights that are attached to the receiver. Next put pure water into the jars,—No. 1 two-thirds full; Nos. 2 and 3 within one and a half inches of the top. Into jar No. 2 put a stick of caustic potash.

Arrange the jars in line, and connect them by tubing as shown in the cut. The tube from the retort must connect with the *long* pipe of jar No. 1, and so on. Always be sure that the *long* pipe of each jar is next the retort. When properly arranged, a current of air blown into the tube intended to connect with the retort will cause the water to bubble in jars Nos. 2 and 3, and, the spigot to which No. 3 is attached being open, the receiver will begin to rise.

Put into the retort the quantity of ammonia intended to be used (1 pound will make about 30 gallons of gas). Connect the long pipe of the first jar to the retort by rubber tubing, so that the condensed steam may run into it. Now apply the heat *gradually*, and *watch* the process, being careful not to overheat the ammonia, which will be known by its violent boiling, instead of the gentle bubbling which indicates the proper temperature. Do not make gas faster than 30 gallons per hour.

The heat should be shut off before the ammonia is quite all decomposed, in order to avoid breaking the retort; and when the gas has ceased to come over, the retort should be disconnected from the tubing, and the receiving spigot closed.

It will be understood that the first jar is merely to receive the drip; the use of the water is simply to keep the jar cool. Some recommend placing this jar into a bucket of cold water.

The inhaling-tube is attached to the spigot at the top of the holder.

The register indicates the number of gallons of gas in the holder, as well as the quantity inhaled.

The water in jars Nos. 1 and 3 should be changed every time the gas is made; that in No. 2 about once a month, when fresh caustic potash should be added. The water in the holder will keep sweet a year or longer if gas is made frequently.

PHYSIOLOGICAL ACTION.—Although nitrous oxide has been used enormously as an anæsthetic, and many papers have been written upon it, yet our knowledge of its physiological action is due to three or four observers. When pure nitrous oxide gas is inhaled for from half a minute to three minutes, insensibility is produced, preceded in many cases by decided evidences of excitement. Some persons under its influence will sink quietly away into unconsciousness, but others will become hilarious, erotic, or pugnacious, and be restrained only by force. During the stage of anæsthesia the patient presents the appearances of asphyxia.

It is probable that the paralysis of function invades the different portions of the nervous system in the same order as does that caused by ether; but we have no positive knowledge upon the subject. A single experiment of Dr. Amory (*New York Medical Journal*, Aug. 1870) indicates that upon the conducting power of the motor nerves nitrous oxide exerts very little or no influence. No studies whatever have been made of the condition of the circulation before anæsthesia is produced. But if, as is almost certain, the anæsthesia is only an asphyxia, the well-known circulatory phenomena of that state ought to be present. Confirmation of this has been afforded by

Dr. Amory, who, by means of a cerebrometer set into the skull of the dog, found that during the period of unconsciousness the cerebral pulsations are very decidedly lessened, and finally abolished, although the cerebral pressure is increased. This would seem to prove that the capillary cerebral circulation is checked and finally arrested, but that the amount of blood in the cerebrum is not lessened.

It is well established that the gas is not capable of yielding its oxygen so as to support life. A taper will burn in it, it is true, but its decomposition is due to the high heat, and at the temperature of the body the compound is a stable one. MM. Jolyet and T. Blanche have found (*Archives de Physiologie*, July, 1873) that seeds will not germinate in it, and that animals (frogs, sparrows, guinea-pigs, rabbits) live no longer in an atmosphere of pure nitrous oxide than in one of nitrogen. Even Dr. Colton, who maintains the absurdity that nitrous oxide produces hyperoxygenation of the blood, states (*The Physiological Action of Nitrous Oxide Gas*, Philadelphia, 1871) that in an atmosphere of the gas a mouse will live only from thirty to sixty seconds, a pigeon one to two minutes, a kitten one to two minutes, a frog thirty to sixty minutes,—all dying of asphyxia.

The French observers above named affirm that nitrous oxide has no effect upon the system; that the phenomena induced are simply due to deprivation of oxygen. The series of facts which they have experimentally proven, and upon which their conclusions are based, are: 1. An animal lives no longer in nitrous oxide than in nitrogen; 2. Anæsthesia occurs at the time that the blood of an animal becomes black; 3. Animals breathing an air containing sixty to eighty per cent. of nitrous oxide, and twenty to forty per cent. of oxygen, are unaffected; 4. The analysis of the blood of two dogs yielded the following results:

No. 1. Conscious.		No. 2. Unconscious.	
Carbonic acid . . .	46 per cent.	Carbonic acid . . .	36.6 per cent.
Nitrous oxide . . .	29 per cent.	Nitrous oxide . . .	34.6 per cent.
Oxygen	19.7 per cent.	Oxygen	3.3 per cent.

and other analyses showed that the coma was not developed until the oxygen in the blood was reduced to three or four per cent. It is evident that if the above analyses are, as from their reports they appear to be, reliable, the anæsthesia is not due to the presence of carbonic acid in the liquor sanguinis, since nearly ten per cent. more of that gas was present in the blood of the conscious (No. 1) than in that of the unconscious dog (No. 2), and also that it is more rational to believe the decrease in the oxygen, rather than the slight increase in the amount of the nitrous oxide, made the difference between consciousness and unconsciousness.

In this connection the very careful experiments of Dr. Amory are most interesting. He found that during nitrous oxide narcosis the amount of carbonic acid exhaled from the lungs is only two-thirds of that eliminated before the inhalation, and that immediately after the recovery of consciousness less than one-third the normal amount of carbonic acid is given off.

This certainly is corroborative of the conclusions of the French observers, which have also received confirmation from the experiments of Mr. Elihu Thomson (*Philadelphia Medical Times*, November 15, 1873), who found that animals in an atmosphere of hydrogen and of nitrogen, and also in vacuo, suffered symptoms precisely similar to those caused by the inhalation of pure nitrous oxide; also, that in man the inhalation of pure nitrogen causes the symptoms of nitrous oxide narcosis, except that the sense of exhilaration is absent; finally, that nitrogen, hydrogen, and nitrous oxide, as well as a vacuum, are rendered capable of supporting life if a proportion of oxygen approaching that existing in common air be introduced. Dr. C. A. MacMunn (*The Spectroscope in Med.*, London, 1880, pp. 73, 75) finds that when an animal is killed by nitrous oxide the arterial blood gives only spectrum lines of reduced hæmoglobin, whilst after chloroform those of oxyhæmoglobin are very apparent.

The evidence so far cited would seem to prove that nitrous oxide produces anæsthesia by causing asphyxia; but the phenomena of mechanical asphyxia are asserted to be different from those caused by the gas. In the experiments of Krishaber (Lyman, *Artificial Anæsthesia*, New York, 1881, p. 315) the circulation was found to be very differently affected by mechanical asphyxia and the inhalation of nitrous oxide. Prof. Paul Bert, of Paris, believing that the production or non-production of anæsthesia by nitrous oxide depends upon its tension in the blood, devised an apparatus by means of which the patient could have administered to him nitrous oxide gas, mixed with an equal amount of oxygen, under a pressure of at least two atmospheres. The result is said to be very satisfactory, and the method to be at present extensively used in Paris. The objections to it are the expensiveness and cumbrousness of the apparatus. It is plain that the method in which nitrous oxide acts cannot as yet be considered as positively determined, and that the subject offers a very good field for research.

Therapeutics.—As an anæsthetic, nitrous oxide is chiefly valuable when short, minor operations are to be performed. The rapidity with which insensibility is induced, and with which it disappears, combines with the general absence of after-effects to enhance the popularity of the gas. When, however, an operation requiring some little time for its performance is intended, ether is far preferable. Nitrous oxide has been administered to many thousands of persons, and until recently no deaths at all attributable to it have occurred. Four have, however, been reported within a short time. In one of these (*Dental Cosmos*, editorial, June, 1872) it is doubtful whether the gas had anything to do with the fatal result, or, indeed, whether it was really administered. In the other instance (*Brit. Journ. Dent. Sci.*, Feb. 1873), death from asphyxia, apparently induced by nitrous oxide, occurred in a healthy man. In the third, death is asserted to have been produced by syncope (*Brit. Med. Journ.*, i., 1877, p. 460). For the fourth case, see *Ibid.*, 1883, ii. 729. The opinion of Dr. Cartwright (*Lancet*, 1876, 689) and of Dr. W. Ottley (*Ibid.*, 1883, i. 95), that in case of heart disease permanent increase of the cardiac weakness is caused by nitrous gas inhalation, is certainly not established.

Nitrous oxide is best administered from an india-rubber bag, which should contain at least eight gallons. The mouth-piece should always be made with two valves, so that the expired gas will be thrown out into the air, and not back into the bag.

ETHER—ETHYL OXIDE. ($C_4H_5O - C_4H_{10}O$.)

Ether is a colorless, very volatile liquid, obtained by the dehydration of alcohol by sulphuric acid. It is very inflammable, as is also its vapor, which is two and a half times heavier than air. It is freely soluble in alcohol, and is itself a powerful solvent. Its odor is strong and peculiar; its taste hot. Its specific gravity, when pure, is 0.713, and its boiling-point 95° F. It is officinal in two forms.

ÆTHER—ETHER. U. S.—This ether contains a large percentage of alcohol, and has a specific gravity of 0.750. When shaken with an equal bulk of water, it loses from one-fifth to one-fourth of its volume. A test-tube full of it held in the closed hand should *begin to boil* on the addition of a piece of broken glass. Any specimen which does not conform to these requirements probably contains an overplus of alcohol or of water.

ÆTHER FORTIOR—STRONGER ETHER. U. S.—This ether should have a specific gravity of 0.728, should not lose more than one-eighth of its volume when shaken with an equal bulk of water, and in a test-tube held in the closed hand should *boil vigorously* on the addition of broken glass.

PHYSIOLOGICAL ACTION.—The first effects of ether when inhaled are burning in the fauces and a feeling of strangulation, both due to the local impression of the irritant vapor. The first indications of its systemic action are a sense of exhilaration and a lightness in the head, associated with a roaring or buzzing in the ears. These are soon succeeded by a feeling of the immediate surroundings being afar off, and this soon fades into semi-unconsciousness, with visions and illusions. These are of various characters, and are often accompanied by a species of delirium. Some patients weep, others laugh; some shout, some pray, some rave, and some become exceedingly pugnacious. In rare instances, the dreams become erotic; and cases are on record in which there were distinct evidences of the occurrence of a complete venereal orgasm. In this stage, the patient in most cases may be more or less perfectly aroused. There is rarely sufficient anæsthesia for practical purposes before the period of complete unconsciousness.

The second stage of ether-narcosis may be considered to commence with the complete loss of consciousness. In most cases, some degree of muscular rigidity is at first still present, but soon passes off, and the patient lies relaxed and quiet, with slow, regular, automatic respiration. The occurrence of stertorous respiration, due to a paresis of the muscles of the palate, shows that the stage of muscular paralysis is being reached. It should, except in very rare cases, be the signal for the immediate withdrawal of the anæsthetic

The face during etherization is reddish; marked pallor and lividity are respectively important indications of failure of the heart's action and failure of respiration. The stage of excitement generally lasts only a few minutes, but in some cases is prolonged, and in nervous women may pass into a violent fit of hysterics, which soon yields, however, to a persistent use of the anæsthetic. The pulse is quickened and increased in force by ether, and it will often maintain itself during a prolonged narcosis. If the vapor of ether be taken in a concentrated form, there is usually in the beginning a momentary arrest of respiration accompanied by a decided sense of suffocation, evidently the result of the irritant action of the vapor upon the upper air-passages. So soon as this has passed off the respirations are usually accelerated as well as deepened; but as the stage of anæsthesia is reached they become slower, and, if the inhalation of the ether be persisted in, they grow not only more and more distant, but also more and more shallow, until they are gradually extinguished. The respiratory phenomena seem to be the same in the lower mammalia as in man. It was noticed by Kratschmer (*Sitzungb. Wiener Akad.*, 1870, Abth. ii.) that in the rabbit ether, when inhaled through the nose, produces at first a momentary arrest of respiration in expiration. He also found that section of the vagi did not prevent this arrest, but that section of the trigemini did; also that the arrest never occurred when the ether was given through a tracheal fistula. This would appear to show that the phenomenon was a reflex one, due to the irritation of the peripheral ends of the trigemini. Its importance is much increased by the consentaneous spasm of the glottis, noticed by Kratschmer. It is possible that some of the accidents happening early in human anæsthesia are the result of such spasm. As stated by Dr. P. Knoll (*Sitzungb. Wiener Akad.*, Oct. 1876), the alterations of respiration are sometimes replaced by very irregular breathing. In either case, if the inhalation of ether be persisted in, the respirations, at first quickened, grow slower and slower, and less and less deep, until they are gradually extinguished. Dr. Knoll experimentally determined that these later respiratory changes are not interfered with by previous section of the vagi; that they follow the injection of the narcotic into the blood; that they are not due to disturbances of circulation, or to a deprivation of the respiratory centres of their oxygen; and logically concludes that they are produced by a direct action of the drug upon the centres, at first stimulant in its character, but subsequently depressant.

According to Prof. Eulenburg, in the beginning of anæsthesia produced either by ether or by chloroform, the patella reflex in man is increased; but whilst this increase soon disappears when chloroform is employed, with ether it endures even into the narcosis (*Hoffmann und Schwalbe*, 1883, p. 117).

Upon the lower animals ether acts as upon man, and it has been shown by Claude Bernard that the most primitive infusoria are susceptible to its influence (*Le Progrès Méd.*, 1876, p. 77).

As the functions of the cerebrum are affected before those of the other portions of the nervous system, it is very apparent that the brain is especially sensitive to the narcotic. Flourens (*Comptes-Rendus*, vol. xxiv., 1847, pp. 161, 242, 253, 340) found that, at a certain stage of etherization, pricking of the anterior or motor nerve-roots caused motor disturbance, although the posterior or sensory portions of the spinal centres were completely insensible. After a more prolonged inhalation, the anterior or motor centres also failed to respond to mechanical irritation, although the functions of the medulla oblongata were regularly performed, and stimulation of its anterior centres gave rise to motor disturbance, and pricking of its sensory portions even caused manifestations of pain. When the inhalation of ether was maintained for a sufficient time, the sensory and finally the motor functions of the medulla oblongata were compromised, and death from paralysis of the respiratory centres ensued.

Longet (*Archives Générales*, 4e sér., tome xiii. p. 374) in part confirms and in part questions the results of Flourens. He states that he has found the sensory functions abolished very early, but has never failed in any stage of the narcosis to get a response from the anterior part of the cord. These apparently different results are simply due to the fact that, whilst Flourens used only mechanical stimuli, Longet employed powerful galvanic currents.

Flourens was substantially correct, and the order of the involvement of the nerve-centres in man and animals is—first the cerebrum, next the sensory centres of the cord, next the motor centres of the cord, next the sensory centres of the medulla oblongata, and finally the motor centres of the medulla oblongata.

That ether is capable of impressing the nerves seems established by the experiments of Longet (*loc. cit.*, p. 382) and of Serres (*Archives Générales*, 4e sér., tome xiii. p. 433). These observers found that the direct application of ether to a nerve produced a paralysis of the sensory fibres of that nerve; so that pinching the nerve below the point of application caused no pain, although voluntary movement was preserved, and galvanization of the nerve-trunk above the point of application induced spasms in the tributary muscles: *i.e.*, the power of conducting an impulse downwards was preserved, that of conducting it upwards was lost. By a longer application of the anæsthetic the function of the efferent as well as of the afferent fibres was abolished, temporarily at first, but, if the application were persisted in, permanently. Practically, however, inhaled ether has no influence upon the nerve-trunks, because the nerve-centres are so much more sensitive to its influence that their functional power is abolished before the nerves are affected. Indeed, Conly (*Soc. de Biologie*, February 13, 1876) found that in animals killed by ether, chloroform, or chloral the motor nerves and muscles preserve their function longer than in animals killed by sudden violence.

Upon the motor system of organic life ether certainly acts, but much less energetically than upon the voluntary system. Thus, after death from ether the vermicular movements of the intestine, although less active than normal, are very rarely, if ever, entirely absent.

It has been shown by the English Chloroform Committee and other investigators that ether increases very markedly the arterial pressure, and that even in a prolonged ether-narcosis there is usually no material diminution of this pressure until manifest failure of respiration has taken place. The rise of the pressure is probably due to an increase of the power of the heart and to a stimulation of the vaso-motor nerves.* Sansom (*Chloroform: its Action and Administration*, p. 92, Phila., 1866) states that the vessels of the frog's web can be seen to contract during the inhalation of ether, and that this vaso-motor spasm is very permanent, and does not yield to paralysis and passive dilatation until the anæsthesia has almost deepened into death. Dr. Bowditch and Mr. Minot also found (*Boston Med. & Surg. Journ.*, May, 1874) that the vaso-motor centres are at first stimulated and afterwards depressed.

Injected even in considerable amount directly into the jugular vein of the mammal, or applied directly to the frog's heart, ether does not seriously depress the heart. When artificial respiration is maintained animals bear an enormous amount of this drug without cardiac failure. When death is produced by ether, the heart generally continues to pulsate for a long time after the arrest of respiration. It is evident that ether is as little of a cardiac depressant as is alcohol.

It is frequently asserted that ether when added to blood coagulates it. A. Schmidt, however, states that the coagulation is due to ozone which has been generated by the ether and is contained in it, since freshly-distilled ether does not coagulate albuminous substances.

The researches of Wittich (*Schmidt's Jahrbücher*, Bd. cxlii. p. 212) and A. Schmidt (*Virchow's Archiv*, vol. xxix., 1864, p. 19) have shown that when ether is added to the blood of horses,† cats, or rats, the red corpuscles disappear in a very short time; and, as their stroma cannot be demonstrated by the aid of reagents, this disappearance is due to its solution. The hæmatin thus set free is dissolved in the serum, but the presence of the ether soon causes it to crystallize. There is no proof that these changes occur to any extent when ether is inhaled; and the usual rapid recovery from the effects of the anæsthetic indicates that there is no profound alteration of the blood.

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* I believe there is a paper "On the Action of Ether on the Circulation" in the *Deutsches Zeitschrift für Chirurgie*, 1874, Bd. iv.; but I have not had access to the volume.

† Schmidt (*loc. cit.*, p. 23) says that sometimes crystallization fails in the blood of the horse.

An imperfect study by Harley of the effect of ether on the gases contained in drawn blood indicates that ether does not exert much influence upon their proportional amounts. It is, however, quite possible that a more thorough investigation would give a different result.

THERAPEUTICS.—As an anæsthetic, ether does not act with the rapidity and pleasantness of chloroform, but it has the advantage of safety. So dangerous is chloroform, and so safe is ether, that there is no excuse for the use of the former agent under ordinary circumstances.[*]

The reason of the safety of ether is that, unlike chloroform, it does not suddenly paralyze the normal heart.[†] It may kill by inducing asphyxia (cases, *British Medical Journal*, vol. ii., 1873; *Chicago Med. Journ.*, 1877, p. 410; *Le Progrès Méd.*, 1877, p. 677; *New York Med. Journ.*, xxiii., p. 179),[‡] but it does so slowly, and in the great majority of cases after warnings which can be overlooked only through the most reckless carelessness.[§] Many of the inconveniences which attend the use of ether can be obviated. Thus, in order to prevent the nausea which often follows the anæsthesia, the patient should avoid eating for at least six hours before the inhalation, and should take from one to two ounces of brandy just before commencing the latter process.

Unlike that of chloroform, the vapor of ether should be administered in a concentrated form. When so inhaled, in most persons it will produce complete insensibility in from three to eight minutes, provided that no uncharged air be admitted during the time named.[§] According to Dr. Snow, air at 80° F. saturated with ether contains seventy-one per cent. of the vapor. This point is probably never reached in the practical use of ether, but the nearer it is approached the more rapid will be the induction of anæsthesia.

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[*] Twenty-seven cases of sudden death from ether are collected by Dr. H. M. Lyman (*Artificial Anæsthesia*, New York, 1881). In most cases the respiratory centres were already enfeebled. Brain tumors, obstructions of the bowels, cancerous tumors, seem even more important contraindications than cardiac disease. In disease of the heart ether is probably the safest of the anæsthetics; but when there is great exhaustion of the nervous system its use requires great caution. Sudden pulmonic œdema, outpouring of bronchial mucus, and fatal cerebral hemorrhage have occurred during, or directly after, the anæsthesia.

[†] For case in which a fatty heart apparently suffered sudden arrest, see *Brit. Med. Journ.*, 1887, ii., p. 602.

[‡] See also *Gaz. Hebdom.*, 1878, p. 583.

[§] Various inhalers have been invented for facilitating the use of ether, but they are very rarely used. For information on these points, see *New York Medical Record*, May 1, 1866, and *New York Medical Journal*, April, 1871. The inhaler of Dr. Allis is probably of real service. See *Philadelphia Medical Times*, vol. iv.

The ordinary method of the administration of ether in Philadelphia is as follows:

Out of stiff paper a cone is made of such size and shape that its base will fit closely over the nose and mouth of the patient. In this cone a napkin, a small towel, or a conical, hollowed-out sponge is to be placed. About an ounce and a half of ether having been poured on the napkin, the cone is to be closely applied to the face of the patient, and *kept there*. If anæsthesia be not complete in four or five minutes, a second dose of ether should be put on the napkin, care being taken that the removal of the apparatus is only momentary. When patients are fastidious, and a few moments are of no importance, the gradual commencement of the inhalation is much more pleasant, as the first choking sensation is thereby to a great extent avoided.

In using ether at night, its inflammable nature must not be forgotten. I have seen fire flash from a candle through some four or five feet of diffused vapor to the sponge. The light should always be *above* the patient, as the high specific gravity of the vapor of ether causes it to fall towards the floor.

Administered by the mouth, ether has been used with advantage in various forms of *colic*, but is generally inferior to chloroform. When, however, as in some cases of *retrocedent* or *internal gout*, there is with the painful gastric and intestinal spasm a condition bordering on collapse, the stimulant properties of ether make it very valuable.

In sudden *sinking-spells*, either from poison or from natural causes, ether, as a powerful and very quickly-acting stimulant, is often indicated. In some cases of this description it may even be administered by inhalation. Of course, under these circumstances its influence should not be carried nearly to the point of producing anæsthesia.

As an *anthelmintic*, ether has been used by MM. Bourdier and Lortet with success against the *tape-worm*. For this purpose, an ounce and a half may be administered at once, followed in two hours by a full dose of castor oil.

In *hysteria*, *neuralgia*, *nervous headache*, and *spasmodic neuroses*, such as *hiccough* and *asthma*, ether is occasionally employed with benefit.

When ether is swallowed, it produces a sense of strangulation and choking, which seriously interferes with its use. For this reason, it is best given in capsules, or in ice-cold water. Probably large doses are best administered by putting them, mixed with an equal amount of brandy, on finely-cracked ice before drinking. The dose is from one fluidrachm to half a fluidounce.

Etherization by the rectum has been tried and discarded because of the severe local irritation produced, as well as the slowness of the production of insensibility.

CHLOROFORMUM—CHLOROFORM.

Methenyl Chloride—Terchloride of Formyl (C_2HCl_3—$CHCl_3$).—This substance, which was discovered in 1831 by Mr. Samuel Guthrie, of

Sackett's Harbor, N. Y., is produced by the action of chlorine upon alcohol. It is a colorless, limpid, and neutral fluid, which is for practical purposes uninflammable, although it can be made to burn with a greenish flame (*Fownes's Chemistry*, Am. ed., 1869, p. 566). Its taste is hot and sweetish; its odor fragrant and peculiar. It is soluble in alcohol and in ether, but when dropped into water it sinks, if pure, as transparent globules without milkiness. The alcoholic solution, when moderately diluted with water, forms an aromatic, sweetish liquid. It is antiseptic, but does not coagulate albumen.

In the U. S. Pharmacopœia it is officinal in two forms.

CHLOROFORMUM VENALE—COMMERCIAL CHLOROFORM. U. S.—The crude chloroform of commerce. Sulphuric acid, when shaken with it, after a time separates as a stratum of a dark-brownish color. This color is due to a carbonization by the acid of the impurities in the chloroform.

CHLOROFORMUM PURIFICATUM—PURIFIED CHLOROFORM. U. S.—The U. S. Pharmacopœia directs that the commercial chloroform shall be purified by the action on it of sulphuric acid and by subsequent neutralization with carbonate of sodium, and distillation in a retort containing quicklime. Purified chloroform should respond to the following tests: Sulphuric acid shaken with it should not be colored; it should not alter litmus blue, even after it has been exposed in a white glass bottle to direct sunlight for ten hours.

PHYSIOLOGICAL ACTION.—Although somewhat of an anæsthetic, chloroform applied locally is a powerful irritant. On the skin it produces redness and burning; if the evaporation be restrained, vesication is induced by it. Taken into the mouth, it causes a burning sensation, and, when swallowed, a sense of warmth in the stomach.

The vapor of chloroform, when inhaled, produces symptoms seemingly similar to those induced by ether, except that the choking sensations are absent, and that the stage of excitement is generally, but not always, shorter and less violent than that of etherization.

Dr. Snow (*On Anæsthetics*, London, 1858) divides the chloroform-narcosis into four degrees or stages, but the division adopted by Sabarth (*Das Chloroform*, Würzburg, 1866) and most writers seems more useful. This classification recognizes three stages. In the first of these, the symptoms are similar to those of alcoholic intoxication. This stage is generally very short, but in athletic persons, and especially in those who have been intemperate, it may be very long and very violent, and may persist after loss of consciousness. In drunkards, this excitement at times cannot be overcome without grave danger to life. During this first stage, although consciousness is not lost, the sensibility is generally blunted, but very rarely is it altogether annulled. Dr. Coleman (Sansom, *Chloroform*, p. 55, Philadelphia, 1866) states, however, that he has extracted his own teeth without pain; and Dr. Snow relates the anecdote of a child who played with his toys during the operation of lithotomy.

During the second stage, which is that of anæsthesia, the consciousness and sensibility are abolished, the muscles are relaxed, and the patient lies perfectly quiet. This is the surgical stage, during which ordinary operations are performed. As already intimated, in some cases the first and second stages are united, so that violent excitement, muscular spasm, and rigidity may coexist with loss of consciousness and of sensibility.

The third stage is one of profound narcosis, with stertorous breathing, intense muscular relaxation, and abolition of ordinary reflex actions. This is always a condition of danger, and its induction, except under very peculiar circumstances, by chloroform, is absolutely unjustifiable.

The pulse in the first stage of chloroform-narcosis may be quickened, even apparently strengthened; in the second stage it is generally about normal in frequency, but is more or less weakened; in the third stage it may be rapid and weak. Dr. Noel (*Lond. Med. Record*, 1877, p. 457) calls attention to a cervical venous pulse, most marked in the external jugulars, which he asserts frequently occurs during the waking up from chloroformization. He believes it to be a symptom of serious cardiac embarrassment. E. Simonin found that the temperature usually rises during the first stage (.1°–.8°C.), falls slightly during the second or remains above normal, and falls decidedly during the third stage (*Centralb. Chirurgie*, 1877, p. 234).

In man the first arrest of respiration, so obvious in etherization, rarely if ever occurs. This is probably in great measure owing to the chloroform vapor, as employed, being much more dilute than the ether vapor. The experiments of Holmgren, Kentschmer, and others have shown that upon the lower animals the respiratory action of chloroform is similar to that of ether (see p. 281), excepting in that it is much more intense.

Dr. Baudin (*Le Progrès Méd.*, Sept. 1874) called attention to the pupil as a guide in chloroformization, stating that, although at first it is uniformly dilated, afterwards it is uniformly immovably contracted, and that this is the period for operating. Schläger is in accord with Dr. Baudin; in one hundred and twenty out of one hundred and twenty-two cases observed the pupil was dilated during the stage of excitement, during complete anæsthesia, narrowly contracted. He also states that if during anæsthesia the pupil returns to normal more chloroform is required, but if it suddenly dilates danger is imminent. At present, however, the condition of the pupil cannot be considered a safe guide in anæsthetization. Dogiel (*Reichert's Archiv für Anat.*, 1866) affirms that in rabbits, during the stage of excitement, the pupil is contracted; during anæsthesia, dilated. Prof. Schiff has strenuously combated the conclusions of Baudin; and in a very careful series of experiments on animals Dr. W. H. Winslow found that the state of the pupil varies very greatly in the same stage of anæsthesia. Thus, in complete anæsthesia, sometimes the pupil was widely dilated, sometimes contracted; and death sometimes occurred with a dilated, sometimes with a contracted pupil; in the former case probably being syncopal, in the latter asphyxial (*Philad. Med. Times*, vi., p. 275).

The action of chloroform on the nervous system, like that of ether, is chiefly upon the brain and spinal centres. Carter (*British Medical Journal*, Feb. 1867) found that very decided anæmia of the brain can be seen in animals subjected to its influence after the cerebrum has been laid bare; and accident in man (*Amer. Journ. Med. Sci.*, 1860) has furnished the corroboration of his experiments. Bernstein (*Schmidt's Jahrbücher*, Bd. cxlii. p. 227) has demonstrated that its action on the peripheral nerves is very slight. He found that there was no perceptible difference in the conducting power of the two ischiatic nerves of a frog, chloroformed after one of its iliac arteries had been tied. It is doubtful how far the muscular excitement of the second stage is due to real spinal exaltation and how far it arises from other causes. Bert asserts (*Comptes-Rendus*, t. lxiv., 1867) that it is purely psychical, and that there is during the production of anæsthesia a steady lowering of reflex activity. He rests this assertion upon the fact that, in animals chloroformed after section of the cord, there is no motor disturbance below the point of section,—a fact which certainly demonstrates at least that the muscular excitement and the convulsions are cerebral.

In some animals the first effect of the inhalation of chloroform upon the circulation is a decrease in the frequency of the heart's action. Dogiel believes that this is due to a stimulation of the inhibitory centres, because he has found that it does not occur after section of the vagi. The after-increase in the rapidity of the pulse appears to be due, at least in part, to paralysis of the inhibitory centres, upon which chloroform seems to act as upon the oculo-motor centres, producing in them at first excessive functional activity, but afterwards functional paralysis. Both Kentschmer and Knoll (*loc. cit.*, p. 11) have noticed in rabbits, when either ether or chloroform is inhaled through the nose, a momentary rise of arterial pressure corresponding to the arrest of respiration, and, like it, evidently produced by irritation of the peripheral trigeminal branches.

The very careful experiments of the English Chloroform Committee (*Med.-Chirurg. Trans.*, vol. xlviii. p. 326) proved that after the first half-minute of the inhalation of chloroform there is a progressive lowering of the arterial pressure. It would, *a priori*, appear probable that this is to some extent due to a vaso-motor paralysis; but Sansom and Harley state that there is a spasm of the small vessels, which can be readily seen to occur in the web of the frog during chloroformization. Not until the third stage is reached, according to these authors, do the vessels relax into dilatation. If these observations are correct, chloroform first stimulates and afterwards depresses the vaso-motor centres. Elsewhere in the present work I have dwelt upon the fallacies of the observations of such as those just quoted, and the experiments upon arterial pressure of Prof. H. P. Bowditch and C. S. Minot (*Boston Medi-*

cal and Surgical Journal, May, 1874) appear to prove that the fall of pressure is in part due to a paralysis of the vaso-motor centre. They found that after the exhibition of the drug in curarized animals galvanization of a sensitive nerve is followed by no rise of pressure, or a very slight one, and that compression of the carotids did not cause the customary vaso-motor spasm and rise of arterial pressure.

On the heart itself chloroform undoubtedly exerts a steady, powerful depressing influence. Injected into the jugular vein, it instantly arrests the heart's action and destroys its muscular irritability.* Even the vapor of chloroform, when locally applied to the exposed heart, paralyzes it (*Edinb. Med. Journ.*, 1842). When artificial respiration is maintained the effect of chloroform upon the heart is very apparent (*Journ. Anat. and Physiol.*, xiii. 226). It is, therefore, demonstrated that chloroform applied in a sufficiently concentrated form *destroys the contractile power of the heart-muscle.*

The respirations may at first be rendered slower by chloroform, but after a time are generally quickened, and as the inhalation is persisted in they become more and more shallow, irregular, and distant, and finally cease.

In animals, without doubt, chloroform, when inhaled, usually produces death by abolishing the functional power of the medulla oblongata and thereby arresting respiration. It has been denied that chloroform-vapor ever kills animals in any other way.† This is, however, a mistake.‡ If the chloroform vapor be administered in a very dilute form, the heart generally continues to beat for a long time after the cessation of respiration. If the vapor have been less diluted, cardiac and respiratory action may cease almost simultaneously. If the vapor have been administered in a concentrated form, arrest of the heart's beat may precede arrest of respiration.§

When death is produced by chloroform in man, it is generally by cardiac arrest, sometimes by asphyxia. That syncope occurs proportionately more frequently in man than in animals, is simply because this form of death is sudden and unexpected. Asphyxia comes on gradually, so that in man the threatening symptoms are perceived, and death is averted by prompt measures. In animals, however, the object being to kill, nature is allowed to take its course.||

The evidence is not at present sufficient to enable a positive determination as to whether the action of the anæsthetic upon the heart, when a sudden fatal syncope is produced, is a direct one, or whether it is a reflex one (T. D.

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* Glover (*Edinb. Med. Journ.*, 1842), Gosselin (*Arch. Gén.*, 1848), Anstie. H. C. Wood.

† See, especially, report of the French Chloroform Commission. Sabarth, *Das Chloroform*, p. 44.

‡ Consult Snow, *On Anæsthetics*, p. 111; Anstie, *Stimulants and Narcotics;* Richardson, *Medical Times and Gazette*, 1870; Chloroform Committee, *Medico-Chirurgical Transactions*, vol. xlvii.; Vulpian, *Leçons sur l'Appareil Vaso-Moteur*, vol. ii. p. 157.

§ Compare *Journ. Anat. and Physiol.*, xiii. 226.

|| For proof that cardiac death does occur among animals, see *Jour. Anat. and Physiol.*, xiii., p. 224.

Lente, *Psychol. and Med. Legal Journal*, Feb. 1875), due to an irritation of the peripheral filaments of the pulmonic nerves. Certainly those who believe it to be reflex have as yet brought forward no proof of their theory. As chloroform does act directly upon the heart, it seems to me wiser to hold to its direct action until it has been demonstrated that it is impossible to produce syncope after division of the par vagum. The mere rapidity of the occurrence is of little importance, as pulmonic absorption is practically instantaneous and the blood goes directly from the lungs to the heart. What is true of the theory of reflex syncope is also true of various other theories which have been brought forward to account for the chloroform deaths. I think they are unnecessary and unproven, although some are ingenious, and it is possible that death may take place at times in the way they suggest. Want of space prevents my doing more than giving references to the most important papers.*

According to Harley (*Physiological Transactions*, London, 1865), blood to which as little as five per cent. of chloroform has been added becomes very liquid and of a bright arterial hue. After a time crystals form in it. Boettcher (*Virchow's Archiv*, vol. xxxii. p. 126) was, I believe, the first to study these changes closely. The first alteration noticeable in the red blood disks is a diminution of their size, which A. Schmidt and F. Schweiger-Seidel (*Berichte d. könig. sachs. Gesellsch. d. Wissensch., math-phys. Kl.*, 1867, p. 190) assert to be due to contraction, because when blood is treated with water until the red globules disappear, and carbonic acid gas is passed through the liquid until they reappear, on the addition of chloroform the sharply-contoured bodies will be seen to undergo marked contraction. As was first shown by Boettcher (*loc. cit.*, p. 127) and confirmed by Schmidt and Schweiger-Seidel, chloroform alone produces no other alteration than contraction in the red blood-disks. If, however, air be admitted to blood containing chloroform, the corpuscles rapidly disappear, dissolving in the serum, out of which, after a time, hæmatin crystallizes. Both of the authorities quoted believe that the latter changes are due to oxidation.

Boettcher states (*loc. cit.*, p. 129) that chloroform-vapor mixed with air converts enough of the oxygen of the latter into ozone to react with iodinized-starch paper; and Schmidt and Schweiger-Seidel have found that an excess of carbonic acid in the blood interferes with the changes caused by chloroform. From these facts it seems probable that their opinion as to the nature of the blood-changes is correct. Harley (*loc. cit.*) has studied the effect of chloroform on the absorption of gases in the blood. He states that when chloroform is added to fresh blood, and the mixture allowed to stand for twenty-four hours, a marked increase takes place in the proportion of oxygen and a lessening in that of carbonic acid. This is in accord with the theory just mentioned; for, after the complete oxidation of the hæmato-globulin brought about by the chloroform, further consumption of oxygen could not occur, and, as it continued to be absorbed from the air, it would accumulate instead of being converted into carbonic acid.

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* Richardson, *Medical Times and Gazette*, 1870. Andrew H. Smith, *New York Medical Journal*, 1871, p. 46. Consult also J. C. Reeve, *American Journal of the Medical Sciences*, Oct. 1867; Henry M. Gibbons, Jr., *Pacific Medical and Surgical Journal*, June, 1869; Snow, *On Anæsthetics;* Sansom, *On Chloroform;* and O. W. Copeland, *Philadelphia Medical Times*, p. 550, 1874.

How far, during ordinary narcosis, chloroform produces the changes just described in the blood, is somewhat uncertain; but it would seem very improbable that they occur to any great extent. A very sensitive test of the destruction of the red disks in the body is found in the production of icterus; and icterus never follows anæsthesia. On the other hand, Husemann (*Schmidt's Jahrbücher*, Bd. cli. p. 84) intimates, on what authority I do not know, that after anæsthesia bile-acids appear in the urine; and Bert (*Journal of Anatomy and Physiology*, May, 1870) has found that the oxygen of the blood undergoes during anæsthesia an increase, such as Harley has found to happen when chloroform is added to blood outside of the body. Nothnagel (*Berlin. Klin. Wochensch.*, 1866) found in rabbits, after subcutaneous injections of chloroform or ether, bile coloring matter in the urine; but Kappeler (*Die Anarsthetica*, Stuttgart, 1880), in twenty-five cases of chloroform narcosis, was not able to obtain a trace of biliary coloring matter (*Zeitschrift f. Physiolog. Chem.*, viii.).

Chloroform is undoubtedly, at least in part, eliminated as chloroform escaping with the breath, also with the urine. Fubini (*Moleschott's Untersuchungen zur Naturlehre*, Bd. xiii. 1882) found it in the urine five hours after its inhalation. Dr. A. Zeller believes that it is in part decomposed, because he has found the chlorides in the urine nearly doubled by its inhalation (*Zeitsch. f. Physiolog. Chemie*, Bd. viii. p. 74).

Albuminuria has been noticed both in animals and man after chloroform narcosis (*Gaz. Hebdom.*, Fev. 1884, 104; also *Brit. Med. Journ.*, 1883, ii. 623). It is affirmed, also, that astigmatism has been produced by chloroform inhalations (*Brit. Med. Journ.*, 1883, ii. 476).

THERAPEUTICS.—As an anæsthetic, chloroform possesses the advantages of quickness and pleasantness of operation, smallness of dose, and cheapness. These advantages are, however, so outbalanced by the dangers which attend its use, that its employment under ordinary circumstances is unjustifiable. It kills without warning, so suddenly that no forethought or skill or care can guard against the fatal result. It kills alike the robust, the weak, the well, and the diseased; even the previous safe passage through one or more inhalations is no guarantee against its lethal action. Statistics seem to indicate a mortality of about one in three thousand inhalations;* and hundreds of utterly unnecessary deaths have been produced by the extraordinary persistence in its use by a portion of the profession. It ought never to be employed except under especial circumstances, as when a speedy action is desired in *puerperal eclampsia*, or when the bulkier anæsthetics cannot be transported, as in the field during war-time.

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* See Richardson, *Medical Times and Gazette*, 1870; Henry M. Gibbons, Jr., *Pacific Medical Journal*, June, 1869; Squibb, *On Anæsthetics*, *New York Medical Journal*, April, 1871. Lyman has collected 342 cases of death from chloroform against 27 from ether, and gives the ratio of death in anæsthesia, chloroform, 1: 5860; ether, 1: 16,542. Nitrous oxide

In obstetric cases, chloroform has been used even by those who give the preference to ether in surgery. So far as I know, no death has as yet occurred from chloroform during *parturition*, although alarming effects have been induced. The excitement of child-birth does seem to fortify the system against the deleterious influence of chloroform. But even in these cases I think ether is just as useful as, and much safer than, its sister-anæsthetic.

Various mechanical inventions have been made for the administration of chloroform; but these inhalers do not appear to offer any advantages over the simple napkin, and, at least in this country, are rarely, if ever, used.* A handkerchief or towel may be folded into a bird's-nest shape, and twenty or thirty drops of the anæsthetic be put upon this and then held close to the mouth. Dr. Simpson advises that a towel be laid over the mouth and nose, and the chloroform slowly dropped upon this until anæsthesia is induced. Whatever plan be employed, it is of vital moment that the vapor be well diluted: not more than three and one-half per cent. of it should be contained in the inspired air.

When administered by the mouth in sufficient quantity, chloroform produces symptoms similar to but much more permanent than those which it causes when inhaled. It is, however, very rarely, if ever, used in this way for its constitutional effect, but is sometimes of advantage in severe *neuralgia*. When quinia for any reason cannot be administered in an *ague*, a sufficient dose of chloroform (fʒss to fʒi) to produce a mild narcosis, given just before the expected time for the recurrence of the chill, will usually abort it.

When chloroform is taken into the stomach, a considerable portion of it is, without doubt, evaporated, so that the intestinal canal becomes filled with the vapor. Chloroform, therefore, when so placed exerts both a local anodyne and a stimulant carminative action. For this reason it is extremely valuable in all cases of *colic*, and it will often even assuage the pain of *colica pictonum*.

Externally, as a rubefacient and anodyne, chloroform is very largely combined with other substances into liniments, which are especially useful in cases of *chronic neuralgic* or *rheumatic pains*.

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appears to be the safest of all the anæsthetics, its ratio, according to Rottenstein, being 1 : 100,000.

The *mixture of ether and chloroform* used by some surgeons is open to the very serious objection that owing to the different volatility of the two agents the percentages of each in the inhaled vapor varies continually. The mixture has in several cases produced death, and is probably no safer than pure chloroform. For latest fatal case, see *Comp.-Rend. Soc. Biolog.*, 1883, iv. 241.

* For a description of inhalers, see works of Sansom and Snow; also Allis, *Phila. Med. Times*, iv.

TOXICOLOGY.—Death may occur at any time during the inhalation of chloroform. In some cases it has seemed to be instantaneous, but generally it is preceded by symptoms such as a change in the expression of the face, which becomes very pale or livid, evident irregularity of the respiration, and failure of the pulse: a shudder, or a violent convulsion, or even a sudden access of maniacal excitement, has been noted in some cases. After death the heart is almost always found relaxed, distended, and its right side filled with blood.

When death is threatened through asphyxia, the alternate dashing of very cold and very hot water upon the face and upper chest is often very efficacious. Artificial respiration should be commenced at once. Faradization of the diaphragm, by pressing one pole firmly against the pit of the stomach and placing the other over the larynx and the root of the neck, has acted very favorably in some cases. Dr. Richardson has shown (*loc. cit.*) that there is a danger of the excitability of the muscle being exhausted by a prolonged use of the galvanic stimulus. The application should not, therefore, be long continued, but should be alternated with artificial respiration. Whenever there is any failure of the heart's action, as is nearly always the case, the body should be laid at an angle of 40°, with the head downwards, so as to favor the passage of arterialized blood to the brain (Dr. E. L. Holmes, *Chicago Medical Journal*, Sept. 1868).*

In artificial respiration, act with the patient, and not against him. He will not cease to breathe at once, and wholly. Enjoin silence; watch the first attempt at inspiration, and at the expiration compress the thorax, aiding its elastic reaction, if absolutely necessary, by Silvester's or some other quiet method. See that the tongue is well forward. Dry external heat must be vigorously used, and the inspired air should be at from 80° to 85° F., or even higher. Frictions and passive motion, to aid in the circulation, must not be forgotten. Efforts at resuscitation should be kept up for at least two hours. Nitrite of amyl has been used as a means of restoring the heart's action, but its power must still be considered entirely *sub judice* (see *N. Y. Med. Journ.*, xxiv., p. 467). Ammonia injected into a vein and digitalis hypodermically given, may be used to stimulate the circulation, but alcohol, if employed at all, must be given very cautiously and with the utmost reserve. Its action upon the heart when in excess is precisely that of chloroform, and the experiments of R. Dubois (*Progrès Méd.*, 1883, xi. 951) show that when alcohol is given freely to the lower animals it intensifies the influence of chloroform, and lessens the minimum fatal dose. In syncope during ether narcosis, alcohol is of still more doubtful value.

Poisoning has been produced by the swallowing of chloroform. The symptoms induced have been stupor, with contracted, or, in later stages, dilated, pupils, and a stertorous respiration, which finally becomes very irregular, shallow, and often distant. The amount necessary to destroy life probably varies greatly. Recovery has occurred after the ingestion of two ounces (Stillé, *Therapeutics*, vol. ii. p. 107), of one ounce (*Canada Lancet*, March, 1874), also of three ounces without vomiting (*Brit. Med. Journ.*, 1882, i. 776). The treatment consists in the use of the stomach-pump and of the various ordinary methods of arousing a narcotized patient, especially the alternate cold and hot douche, artificial respiration, and the very cautious use of diffusible stimuli if required. Death may occur during the narcosis, or the patient may survive this and perish from inflammation of the trachea, œsophagus, and stomach, caused by the local action of the chloroform.

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* I have allowed this sentence to remain as it was in the last edition. Since it was first published, the method has been brought forward as new, and as having originated with Nélaton (*Philadelphia Medical Times*, vols. iv. and v.) The position of the patient is of extreme importance. In severe cases the head should be placed vertically downwards.

The recognition of chloroform as the probable cause of any given death cannot be based upon the post-mortem appearances. Indeed, the latter are of no value in deciding such a question. The anæsthetic may, however, be recovered by distillation of the lungs and blood within a certain period of time after death. As to the length of this time, so far as I am aware, no investigations have been made.

Experiments made at the Philadelphia Hospital and confirmed by Prof. Dolbeau (*Annales d'Hygiène*, Jan. 1874) have proven that persons sound asleep may be chloroformed without their being awakened. Anæsthesia cannot, however, be produced in any one partially awake, or even sleeping lightly, without his knowledge.

Quite a number of professional men have been accused, and some convicted on the charge, of committing rape on females in whom they were inducing anæsthesia. The women, no doubt, believed that they had been violated; but it is certain that in many of the cases, and probable that in all of them, they mistook for the real act the subjective erotic sensations induced by the chloroform or ether. The valuelessness of the testimony of persons as to occurrences during the time of their intoxication with anæsthetics should be recognized by law as a governing principle of evidence.

ADMINISTRATION.—Internally, from fifteen drops to a fluidrachm of chloroform may be given in emulsion, or, as it has recently been stated, dissolved in glycerin (1 to 3). The deep injection of half a drachm of chloroform has been recommended very strenuously by Prof. Bartholow in obstinate *neuralgia*, and has found some favor in France (*Bull. Thérap.*, xciii., pp. 433, 471). In the only case in which I have tried it, one of trigeminal neuralgia, the local symptoms caused by it were so severe as to imperil the life of the patient. The U. S. Pharmacopœia recognizes a *spirit* (*Spiritus Chloroformi*—1 to 10, U. S.), dose, one to two fluidrachms, and a *mixture* (*Mistura Chloroformi*, U. S.). From the commercial chloroform a *liniment* (*Linimentum Chloroformi*, U. S.).

Bichloride of Methylene was introduced to the notice of the profession by Dr. B. W. Richardson (*Medical Times and Gazette*, 1867, p. 478) as an anæsthetic similar to, but more pleasant and possibly safer than, chloroform, and has been rather extensively used in London. It has never been largely employed in this country. There is no way of knowing how many times it has been administered, but nine cases of death from its use are recorded (*British Med. Journ.*, 1883, ii. 104). The detailed phenomena in some of these cases indicate that, like chloroform, the bichloride of methylene kills by paralyzing the heart. It is not probable that it will ever come into general use as an anæsthetic.

The *Bromide of Ethyl* * has been used as an anæsthetic, and at one time bid fair to become very popular. The occurrence of two deaths during its use, however, early arrested its successful career. It is a very prompt anæsthetic, in most cases acting even more quickly than does chloroform, but less agreeably to the patient. Recovery is very prompt. Its action upon the heart is the same as that of chloroform. Injected into the jugular vein, it arrests the heart, and one death produced by it was distinctly by syncope. In some cases it has seemed very irritant. It appears to be quite as dangerous as chloroform, and will probably never be used to any extent in practical medicine.

Bromoform.—According to the researches of Bonome and Mazza, this substance acts as a general anæsthetic both upon man and animals, causing, however, much irritation of the conjunctiva and nasal mucous membrane. The narcotic stage is slowly developed and passes off slowly; the blood-pressure sinks somewhat; the respiration is not disturbed; the irritability of the brain cortex is diminished. Bromoform is said also to be a powerful antizymotic (*Centralb. f. Chirurgie*, 1884, 594). I see no reason for believing that bromoform will be of any value as an anæsthetic. See also *Med. Jahrb. Wien.*, 1883, 497.

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* In a valuable paper (*Amer. Jour. Med. Sci.*, July, 1881) Dr. E. T. Reichert brings much evidence to show that all anæsthetics containing a halogen are cardiac depressants. He makes out his case sufficiently to at least warrant great caution in the use of any such anæsthetic.

CLASS IX.—EXCITO-MOTORS.

In this class are included such drugs as increase the reflex activity of the spinal centres and thereby give rise to disturbance of motility. The only representatives of the class used by the practitioner of medicine are those drugs which contain strychnia as their active principle.

NUX VOMICA—NUX VOMICA. U.S.

The seeds of Strychnos nux vomica, a middle-sized tree growing in the East Indies, whence the drug enters commerce. They are circular, nearly flat disks, a little less than an inch in diameter, covered with very short, satin-like, grayish hairs; internally they are tough and horny, and are possessed of an intensely bitter taste. They contain two alkaloids,—strychnia and brucia,—existing in combination with an acid, the *igasuric* of Pelletier and Caventou, which, according to Husemann, is probably identical with malic acid. *Brucia*, which, unlike strychnia, is not officinal, is readily recognized by the following test. When concentrated nitric acid is added to it, a beautiful scarlet or blood-red color is developed, which becomes yellowish-red, and, by warming, yellow; if to this yellow solution, somewhat diluted, some chloride of tin or sulphuret of ammonium be added, it becomes a beautiful reddish-violet. Physiologically and therapeutically this alkaloid is similar to, but weaker than, strychnia.

The dose of the *extract* (*Extractum Nucis Vomicæ*, U. S.) is from one-fourth to one-half of a grain, given in pill; of the *tincture* (*Tinctura Nucis Vomicæ*—1 to 5, U. S.), fifteen to twenty-five drops; of the *abstract* (*Abstractum Nucis Vomicæ*, U. S.), one to two grains; of the *fluid extract* (*Extractum Nucis Vomicæ Fluidum*, U. S.), two to three minims.

STRYCHNINA. U.S.

As kept in the shops, strychnia is a grayish-white powder, but by slow crystallization from its alcoholic solution it may be obtained in octahedral or in quadrilateral prisms. It is soluble in about seven thousand parts of cold water; in two thousand parts of boiling water; very sparingly soluble in absolute alcohol, ether, and benzine; freely soluble in boiling officinal alcohol, which deposits it on cooling. It is so bitter that it will impart a very intense taste to twenty thousand times its weight of water.

Strychnia yields a very pronounced violet color with many oxidizing reagents. The one most ordinarily employed is a mixture of concentrated sulphuric acid and bichromate of potassium (*Otto's test*). According to Dr. Guy, the test is most delicate if the alkaloid be dissolved in a little concentrated sulphuric acid on a plate, and the bichromate added to it, when a bluish and then violet-purplish color is developed, passing finally into a dirty green. ***Davy's test*** consists in the substitution of a crystal of red prussiate of potassium for the bichromate. ***Marchand*** uses the peroxide of lead; in this case the sulphuric acid should contain one per cent. of nitric acid. Drs. Vrij and Van der Burg say that these tests are about equally sensitive, and are capable of revealing the one sixty-thousandth of a grain of the alkaloid. Either the chlorate or the permanganate of potassium may be used instead of the bichromate; indeed, Dr. Guy claims that the permanganate is preferable to the latter. If the strychnia be in quantity, it may be dissolved in very dilute sulphuric acid, and solution of bichromate of potassium be added, when golden-red needle-like crystals of the chromate of strychnia will separate. These dissolve, with the production of a beautiful blue color, in concentrated sulphuric acid. F. L. Sonnenschein (*Vierteljahresschrift für Prakt. Pharmacie*, 1871) says that if strychnia be dissolved in a strong solution of the sulphate of sesquioxide of cerium a beautiful color is induced, which generally passes into a cherry-red, and so persists for several days. Dr. Filchol's test (*Lancet*, April, 1872) consists in the addition of solution of chloride of gold, and the testing of the precipitate by Otto's method. The ***physiological test*** for strychnia is a very sensitive one. In it a fragment of the suspected extract, dissolved in a little acidulated water, is thrown into the cellular tissue of a small frog, which should afterwards be allowed to swim about freely, so that its unconstrained movements can be watched.

PHYSIOLOGICAL ACTION.—Strychnia acts in the same way upon almost all animals. According to Leube (*Reichert's Archiv für Anatomie*, 1867, p. 630), however, it takes ten times as much to kill chickens as other birds, weight for weight; and among mammals the guinea-pig is very insensitive to it. It has also recently been asserted that on some monkeys it has very little influence (*Boston Medical and Surgical Journal*, 1872). Its local action is that of a slight irritant.*

When taken in quantities just sufficient to produce sensible physiological effects, strychnia in man induces a feeling of restlessness, perhaps accompanied by tremblings in the limbs and some stiffness in the neck and jaws. When a somewhat larger amount has been given, there may be general muscular twitchings and startings, with stiffness and stricture of the throat and chest; formications or other abnormal sensations under the skin may or may not be present. After poisonous doses the symptoms come on usually in from fifteen to twenty minutes, rarely after the hour, with great suddenness; sometimes the convulsions are preceded by partial spasms of the muscles of the extremities, but more often the patient is suddenly thrown down by a general tetanic spasm. In this the body is bent backwards and rests upon the heels and the head, in a condition of profound opisthotonos; the legs are rigidly extended and the feet everted; the arms bent and the hands clenched; the eyes staring, wide open; the corners of the mouth often drawn up so as to produce the *risus sardonicus*. The senses are often sharpened, but ringing in the ears and dimness of vision may be induced if the fits are severe. The face is at first pale, but, if the fit is sufficiently severe and be protracted, it becomes livid from the interference with respiration. Consciousness is not affected, unless when asphyxia becomes so pronounced as to threaten death; in such cases *sometimes* a period of insensibility precedes dissolution, but generally the intellect is clear to the moment of death. The muscles of the jaw are usually the last in the body to be affected, but trismus finally comes on in severe cases. I have seen death occur in this first convulsion in animals; but Tardieu states that he knows of no such instance in man (compare case of Dr. Demme, *Syd. Soc. Year-Book*, 1865–66, p. 441). After a time the paroxysm is at an end, the jaw drops, the muscles relax, and a period of calm comes on, to be succeeded by a second convulsion like the first. These convulsions are excited by the slightest touch, by a draught or breath of air, even by a loud sound; but a firm grasp or hard rubbing of the muscles is frequently grateful. A slight rigidity is sometimes manifest between the paroxysms, but no marked stiffness. The spasms are generally, but not always, very painful. There are often erections of the penis, and the fæces and urine may be passed involuntarily. If the case terminate favorably, the convulsions gradually lessen in intensity, and fade away, leaving the patient exhausted, with a sore, tired feeling in the muscles. After death, post-mortem rigidity is developed very quickly. Autopsies have revealed nothing but the usual congestive lesions of death from asphyxia, and, at times, indications of spinal hyperæmia.

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* For an elaborate memoir on the effect of age on action of strychnine, see *Arch. f. Ges. Physiolog.*, 1884, xxiv. 530. It is affirmed that very young animals require very **large doses to kill.**

In regard to the method in which strychnia produces the above symptoms, it is obvious that the alkaloid is primarily absorbed; and experimental proof seems so superfluous that I will only mention the fact that Masing has found the strychnia in the blood.

It is very plain that convulsions can be produced by a drug in only five ways: first, they may be epileptiform,—*i.e.*, cerebral; second, they may conceivably be due to a stimulation of the peripheral ends of the motor nerves; third, they may conceivably be caused by irritation of the peripheral ends of the sensory nerves; fourth, they may be muscular,—*i.e.*, due to a direct action on the muscles; fifth, they may be spinal.

That the convulsions of strychnia-poisoning are not cerebral, is proven by the fact which has been frequently noted, and which I have confirmed, that they are not affected by section of the cord, or, at least, are only so far affected as to be more severe in those portions of the body removed from the cerebral influence. That they are not due to irritation of the peripheral motor nerves and are not muscular is proven by the experiment of Valentin (*Pathologie der Nerven*, p. 327, Leipsic, 1864), who found that the injection of a solution of strychnia through the blood-vessels of the amputated leg of a frog had no influence upon the muscles. A very beautiful experiment of Brown-Séquard (*Comptes-Rendus*, 1849) confirms this, and also demonstrates that the convulsions do not arise from hyper-excitability of the peripheral afferent nerves. The observer last mentioned found that when the spinal cord was cut just below the origin of the nerves supplying the fore legs of a frog, and all the blood-vessels going to the lower section of the cord were also severed so as to isolate the latter, on the exhibition of strychnia convulsions occurred in the anterior part of the body, whilst in the posterior segment quiet and a normal reflex activity were maintained, although the blood was carrying the poison to every part of it except the spinal cord. The philosophy of this is evident. The anterior section of the cord, receiving the poison, gave rise to convulsions; the posterior section, receiving no poison, maintained its usual status.

This experiment of Brown-Séquard has been repeated a great number of times by MM. Martin-Magron and Buisson (*Journal de la Physiologie*, 1860, t. iii. p. 130) with similar results, excepting that in some very rare instances slight convulsions were induced in the posterior portion of the body. These exceptional phenomena appear to have been due simply to a minute portion of the poison reaching the spine by inhibition, since, when by an operative procedure not necessary here to detail (*loc. cit.*, p. 131) the posterior section of the cord was completely isolated and access of the poison by diffusion rendered impossible, spasms never occurred in the posterior part of the body.

Strychnic convulsions must be spinal, because they do not arise in any of the other possible methods. This conclusion is abundantly confirmed by direct experiment. Thus, Van Deen (*Physiologie de la Moelle épinière*) and Valentin (*loc. cit.*, p. 329) have shown that when the alkaloid is placed upon the spinal cord, and allowed slowly to diffuse itself, the usual convulsions occur, but are at first confined to those muscles whose nerves have their origin near the point of application, and afterwards spread from muscle to muscle as the poison creeps through the cord. Dr. A. J. Spence (*Edinburgh Medical Journal*, July, 1866) has performed similar experiments, with similar results. He first bisected the apex of a frog's heart so as to allow all the blood to drain from the body, and then, cutting through the cranium, laid a little piece of nux vomica within it upon the brain so that the poison would diffuse down through the spinal cord. The result was that first the muscles of the throat, then those of the fore legs, and so on in regular order, were affected.*

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* Some of the phenomena stated by Dr. Spence to have occurred are at present very difficult to explain. Thus, he noted that as the poison traveled down the cord there was a time when irritation of the fore feet caused only spasm in them; later in the experiment, irritation of the front feet caused spasm of both the front and hind feet, although irritation of the latter did not produce other than normal reflex movements; later still in the poisoning came a stage when irritation of the front legs was powerless to cause spasm in the hind legs, although irritation of the latter would now cause spasm in the former.

Spinal Cord.—Claude Bernard (*Leçons sur les Substances toxiques*, Paris) has denied that strychnia produces excitation of the spinal motor centres, because when all the posterior nerve-roots are cut, no convulsions occur, whereas if a single afferent root be allowed to remain, irritation of its peripheral fibrillæ causes general tetanic spasms. Allowing the truth of his experimental fact, his deduction certainly is not warrantable.* The non-occurrence of convulsions may depend upon the fact that the reflex motor ganglionic cells are incapable of originating an impulse, and in strychnia-poisoning are simply in such a condition of over-excitability as renders them exceedingly sensitive to slight irritations and causes them to respond most energetically to peripheral impulses so feeble as not to be felt in health. That the motor centres are acted upon by strychnia is proven not only by the experiments that have been already detailed, but by the following ingenious one of Van Deen (*Physiologie de la Moelle épinière*). That investigator removed the viscera, vessels, etc., from a frog, so as to leave nothing below the second cervical vertebra but the bones, nerves, and muscles; then, opening the spinal cord in the region of the third vertebra, he cut entirely through the anterior columns of the cord, and finally divided all the tissues, so that the anterior portion of the frog was connected with the posterior solely by the posterior columns of the cord. When one or two drops of a solution of strychnia were placed in the mouth of the prepared batrachian, tetanus, confined to the anterior segment of the body, was developed; and it was also found that whilst irritation of the posterior feet caused in them only ordinary reflex movements, in the front legs tetanic spasms were simultaneously induced. It appears to me proven by the evidence adduced in this and the preceding paragraphs that strychnia is a powerful stimulant to the motor cells of the spinal cord; including in this term the whole spinal tract up to the pons varolii. As shown by Spitzka, and confirmed in my laboratory, enormous doses of strychnia injected into a vein kill almost instantaneously without the production of a spasm. Such doses probably kill the nerve-centres just as large doses of a cardiac stimulant overwhelm and paralyze the viscus.

Motor Nerves.—The action of strychnia upon the motor nerves has been a subject of considerable controversy. That the convulsions occur independently of any such influence, if it exist, has been already shown. After death from strychnia, the functions of the motor nerves are always found to be more or less impaired, so that galvanization of the nerve-trunk either produces only very feeble contractions in the tributary muscles, or else none at all.† Of this fact there would seem to be no doubt; it has been attested on the evidence of personal experiment by many observers, among whom are Matteucci (*Traité des Phénom. électro-physiol.*, Paris, 1844), Moreau (*Comptes-Rendus Soc. de Biol.*, 1855), M. Ambrosoli (*Gaz. Méd.*, 1857, p. 525), Wittich (*Bericht Fortschritte Anat.*, 1857, p. 434), Kölliker (*Virchow's Archiv*, Bd. x. p. 239, 1856), and Vulpian (*Arch. de Physiol.*, Nov. 1870, p. 125). Now, it is evident that this absence of response may be due to loss of functional power in either muscle or nerve. Sometimes the muscle may be at fault; but, as Matteucci (*loc. cit.*) insists, and as has been noted by many observers, not rarely—indeed, most generally—in the frog galvanization of the nerve fails to elicit response, although the muscle preserves its irritability. M. Ch. Richet (*Compt. Rend.*, xci. p. 131) determined experimentally that if active artificial respiration be maintained, enormous doses of strychnine injected into the vein of a mammal paralyze the motor nerves. M. Vulpian (*Ibid.*, xciv. 556) has confirmed these results: so that it may be considered proved that in the warm- as well as in the cold-blooded animal strychnine depresses directly the motor nerves.

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* Dr. Spitzka (*Chicago Journ. Ment. and Nerv. Dis.*, vi. 216) affirms that a frog with all the sensory nerve-roots and the nerves of special sense divided still develops tetanus when strychnia is administered. It would be strange if so noted a physiologist as Claude Bernard should make so gross an error in experimentation.

† Dr. W. H. Klapp affirms that he has found in thirty-seven experiments the motor nerve unimpaired in the frog after death from strychnia (*Journ. Ment. and Nerv. Dis.*

It having been proven that the functional power of the motor nerves is destroyed in strychnia-poisoning, the question arises, Is this destruction a direct action of the poison, or is it simply the exhaustion of over-use, due to the intense activity of the nerve during the stage of spasm?

It cannot be gainsaid that the power of the nerve is lessened by the strain upon it during the convulsions; and Kölliker concludes (*Virchow's Archiv*, Bd. x., 1856) that this is the sole cause of the nerve-paralysis, because when he cut the sciatic nerve of a frog and exhibited strychnia the divided nerve would respond to galvanic stimuli after all functional power had been lost in the nerve whose connection with the centres was intact. Granting the experimental fact, it would only prove that contact of the poison was not the sole cause of the motor-nerve paralysis, as it is plain although both nerves suffered this contact, yet the uninjured suffered it plus exhaustion from excessive use. The conclusion is, moreover, opposed by the fact attested by Vulpian (*Archives de Physiologie*, 1870, t. iii. p. 120) and other observers, that an enormous dose of strychnia kills the frog without the induction of

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Oct. 1878). It is inconceivable that all previous observers should be mistaken in their observations. It has been suggested that the effects upon the motor nerves usually attributed to strychnia have been due to brucia contaminating it; and Dr. Robert P. Robins (*Phila. Med. Times*, ix. 228) has found nerves insensitive in animals killed with brucia; a result in accord with the experiments made upon Rana esculenta by Prof. Mounier, of Geneva. Dr. Lautenbach has shown, however, that chemically pure strychnia impairs the function of the motor nerves, and that in some frogs, or under some life conditions, brucia has no effect upon the nerves. It would seem that both of these alkaloids impair the functions of the motor nerves, but that under certain conditions the nerves have greater resisting powers than usual. It is probably different states of health rather than different species of frogs, as believed by Lautenbach, that cause the diversity of results. The possibility of a stray galvanic current being directly transmitted by a nerve to a muscle must also not be forgotten.

spasms by general paralysis, with total loss of power in the nerve-trunks. Evidently in such case the action of the poison on the nerves must be direct.

MM. Martin-Magron and Buisson have investigated (*Journal de la Physiologie*, 1860, t. iii. p. 342) very elaborately this action of strychnia upon the nerves, and the correctness of their experiments and results seems to me scarcely questionable. They found (*loc. cit.*, p. 347) that if the sciatic nerve of a frog were cut and a sufficiently large dose of the strychnia administered, the divided sciatic lost its irritability, although, unless the dose was very large, not so soon as did its fellow. Vulpian (*loc. cit.*, p. 126) has confirmed this; and the opposite result of Kölliker no doubt depended upon his not using sufficiently large doses of the alkaloid or upon his testing the nerve too early. Martin-Magron and Buisson also tied all the tissues of a frog's leg except the nerve, and then, on exhibiting strychnia, found that convulsions ceased in the poisoned much sooner than in the non-poisoned leg, and that at a certain time irritations of the poisoned foot would induce tetanic spasms *only* in the *non-poisoned member*,—proof that the afferent nerve-fibres of the poisoned leg were not affected, and that the motor nerves were paralyzed wherever the poison had access to them; and that to this, not to spinal exhaustion, was due the general paralysis.

M. Vulpian (*loc. cit.*, p. 121) affirms that he has repeated this experiment many times, and always obtained the same result as Martin-Magron and Buisson. It would seem to prove that strychnia in very large doses paralyzes the efferent, but not the afferent nerves; and that the collapse of strychnia-poisoning in the frog is largely due to the affection of the motor trunks, and not to exhaustion of the spinal cord. Again Vulpian (*loc. cit.*, p. 122) found that the nerve protected by tying its vessels preserved its irritability after the non-protected nerve had lost its functional power. The evidence appears to be as complete as it can, and to show that in strychnia-poisoning, at least in the frog, the motor nerves lose their functional power partly through exhaustion and partly through a direct action of the poison upon them. As Fraser has discovered for atropia, Vulpian (*loc. cit.*, p. 128) has found for strychnia: namely, that after a time,—say from some hours to two days,—if the dose has been of the right size, the strychnic paralysis passes off, the motor nerves are found to have regained their power, and the convulsions reappear, and continue hours or days.

Circulation.—Strychnia has a very decided influence upon the circulation. Drs. Richter (*Zeitschrift f. ration. Med.*, 1863, xviii.), Mayer (*Med. Jahrb. d. k. k. Gesellschaft der Aerzte zu Wien*, 1872, p. 112), Schlesinger (*Ibid.*, 1874), and Klapp (*Journal of Mental Diseases*, Oct. 1878) have all found that a decided rise of arterial pressure comes on before or about the time of the first convulsion. The rise is not due to the convulsion or to the interruption of the circulation, as it occurs in curarized animals in which artificial respiration is maintained. Both Richter and Mayer affirm that the small arteries can be seen to contract under the influence of the strychnia, and conclude that the rise of the pressure is due to vaso-motor spasm. Mayer also found that after paralysis of the dominant vaso-motor centres by section of the cord, strychnia produced no rise of the arterial pressure, or if any was caused, it was very slight. A different experimental result has, however, been reached by Schlesinger (*loc. cit.*). This investigator found that the rise after the division of the cord both absolutely and relatively exceeds that produced in the normal animal. It is worthy of note that in three of the fifty experiments made by Schlesinger upon rabbits, the strychnia failed to elevate the pressure after section upon the cord. Schlesinger explains the apparently opposite results reached by himself and by Mayer by the fact that the latter investigator employed dogs, and further states that in six experiments made by himself on dogs, he four times obtained results similar to those of Mayer. Klapp experimented upon the cat, dividing not only the spinal cord, but also all the cardiac nerves of the neck. Under these circumstances no rise of pressure followed the injection of the strychnia. A very plausible explanation of the peculiar results obtained by Schlesinger is that given by Klapp: namely, that he failed to make a perfect section of the cord, Klapp having found that a few fibres are sufficient to carry up the impulse. Further experimentation upon rabbits is necessary before any final judgment can be passed upon the work of Schlesinger, but the drift of the whole evidence is to show that much of the rise of the arterial pressure produced by strychnia upon the normal animal is due to vaso-motor spasm. It is well known that after division of the cord stimulation of a sensitive nerve fails to cause vaso-motor spasm and rise of arterial pressure. Schlesinger found that in the strychnized animal the contrary to this is true. This curious asserted fact receives some support from the experiments of Klapp. In the majority of instances he failed to get a decided rise, but in a few cases he did. The explanation of Schlesinger is that in the normal animal the peripheral impulse can only reach the vaso-motor nerves by first going to the dominant centre, but that strychnia so alters the functional conditions of the spinal cord as to allow the peripheral impulse to play all through the local vaso-motor centres, which undoubtedly are in the cord, and to cause a general vaso-motor spasm by producing innumerable local spasms. This theory may be true, but must yet be considered as *sub judice.*

It has been shown by the experiments of Klapp that the primary stimulation of the vaso-motor centres by strychnia is followed by fall of arterial pressure and vaso-motor palsy; also that very large doses produce an immediate depression of the vaso-motor centres and fall of the arterial pressure.

There is some apparent conflict of testimony in regard to the influence of strychnia upon the inhibitory cardiac nervous system. Dr. Carl Heinemann, who has investigated at some length (*Virchow's Archiv*, Bd. xxxiii. p. 394) the influence of the drug upon the heart of the frog, finds that large doses cause diminished frequency of the cardiac movements, with diastolic pauses. According to his experiments, these phenomena are not due to stimulation of the inhibitory nerves, since they occur after section of the vagi (p. 403), nor are the peripheral vagi paralyzed, since galvanization of one of these nerves causes immediate diastolic cardiac arrest (p. 406). Mayer (*loc. cit.*) has also found that the peripheral vagus is not paralyzed, since he could suspend the action of the heart in the poisoned animal by galvanization of the par vagum. Klapp has also reached results confirmatory of those of Heinemann. On the other hand, Martin-Magron and Buisson affirm (*loc. cit.*, p. 352) that in all of very many experiments, after a greater or less length of time, the pneumogastrics lost their power of transmitting an impulse. The reconciliation of these results is very difficult; possibly Martin-Magron and Buisson employed a strychnia containing very largely of brucia; possibly enormous doses of strychnia do affect the peripheral vagi, but not until very late in the poisoning, although when small doses are employed, even death may occur without very decided paralysis of these nerves. That the different results are not due to the use of different animals is evident, since, although Mayer used hounds, both Heinemann and Klapp employed the same animals as did Martin-Magron and Buisson, viz., frogs. Dr. I. Steiner has found the action of strychnia much more marked when it is placed upon the posterior than on the anterior face of the frog's heart, also that the strychnia acted much more promptly and severely upon the separated sinus venosus than upon the ventricles or auricles, and hence concludes that the strychnia acts especially upon the ganglia of the sinus. His experiments and conclusions have been confirmed by Klapp, and are probably correct.

Upon the *blood* strychnia has probably some action. Harley found that blood shaken for twenty-four hours with air contained 11.33 parts of oxygen and 5.96 parts of carbonic acid; whilst blood treated in a precisely similar manner, except in the addition of strychnia, yielded 17.80 parts of oxygen and 2.73 parts of carbonic acid. He concludes from this that strychnia arrests oxidation in the body; but the deduction seems to me out of all proportion to the fact.

Eye.—The effect of strychnia upon the normal eye has been recently studied by V. Hippel (*Wirkung des Strychnins auf die normale und kranke Augen*, Berlin, 1873) and Cohn (*Wiener Mediz. Wochenschrift*, Nos. 42, 47, 1873), with rather different results. They both, however, found the sharpness of vision increased.[†]

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[*] For the paper of Brunton and Cash showing that strychnine increases the "refractory period" of the isolated frog's heart, see *Proc. Roy. Soc.*, 1883. A consideration of this memoir would require an elaborate discussion of the minute points of cardiac physiology, and, as it would throw at present no light upon the practical use of the drug, is not entered upon.

[†] For the details of their studies the reader is referred to the original paper, or to the abstract in the *Boston Medical and Surgical Journal*, p. 473, 1874.

Elimination.—Strychnine is eliminated with the urine, according to the experiments of Peter von Rautenfeld, unchanged and very slowly (*Inaug. Dissert.*, Dorpat, 1884). P. C. Plugge has found, however, that at least a portion of the strychnine is oxidized and converted into a new substance, which he calls strychnic acid. (For details, see *Archiv d. Pharmacie*, 1883, p. 652.)

THERAPEUTICS.—As a vegetable bitter, strychnia is, of course, a tonic, stimulating to a greater or less degree the digestion, besides acting more universally on nerve-power. But it is more than a mere stomachic: clinical experience has shown that it is a most useful tonic when there is general relaxation and loss of nerve-power. A portion of its value arises, it may be, from its action upon the spinal motor nerve-centres; but in all probability it influences other portions of the cord, affecting the vaso-motor centres, and most probably also the trophic centres, if they exist. Be these things as they may, clinical experience has abundantly demonstrated the value of the drug as a tonic in general *functional atony and relaxation.*

The great influence of strychnia upon the function of voluntary motion early led to its use in cases of *paralysis*, often with the result of doing harm rather than good. Its peculiar physiological action being known, it becomes very evident that it can be useful only when the paralysis is dependent upon, or at least accompanied by, a *depressed state* of the *spinal* or other *motor centres.* Whenever there is *inflammation or irritation of these latter*, strychnia may do great injury by increasing such irritation, and must never be employed. Like galvanism, in *hemiplegia* it can do only a very limited amount of good, and should not be exhibited until irritation from the clot has ceased. Andral and others commend it especially in *lead-paralysis.*

Since attention was so signally called to the value of strychnia in *amaurotic* affections by Nagel, of Tübingen, in 1871, numerous observers have published extended series of cases in which it has been used with strangely-varying results. They have for the most part, however, served to verify the favorable results obtained by Nagel (*Die Behandlung der Amaurosen und Amblyopeen mit Strychnin*, Tübingen, 1871). His sanguine expectations regarding its use in nerve-atrophy have met with disappointment in the hands of other observers. It is now conceded that in atrophy of the essential nerve-structure little is to be expected from strychnia or any other means. It is most useful in cases which have not yet reached the stage of atrophy, but present slight if any ophthalmoscopic changes. The chalky or greenish-white and cupped nerve-entrance is not always, however, sufficient cause for pronouncing the case hopeless, for these appearances are not always safe indications of the amount of injury done to the axis-cylinders. Its value in amaurosis from abuse of alcohol and tobacco is undisputed. Also in amblyopia from disuse,—*e.g.*, in strabismus and paresis,—after the parallelism of the visual axes has been restored, under its use normal sharpness of vision is much more rapidly attained. In cases where the ophthalmoscope reveals but slight change in the retina and nerve,—*e.g.*, slight striation of retina around the disk, the margin of which is somewhat obscured, or in those disturbances of the anastomotic circulation at the nerve-entrance, with or without diminished sharpness of central vision and contraction of the field, —strychnia is of marked benefit. The distressing headache and giddiness associated with these nerve-troubles which thus manifest themselves in the eye are frequently relieved by the use of strychnia, even though the nerve is quite atrophied and the eye blind. There is much difference of opinion as to the method of its administration, but better results in the hands of most observers follow its hypodermic use. The temple would seem to be a better locality than the arm, as improvement in the corresponding eye has been frequently observed, while its fellow remained as before. It should be given in gradually-increasing doses, being governed by the tolerance of the action of the drug. Commencing with one-thirtieth of a grain, it can, usually, in a few weeks be carried up to one-tenth or even one-fifth of a grain once or twice daily, these doses causing only a twitching in the calves of the legs, or a slight sense of constriction about the throat, coming on in from ten to fifteen minutes after their administration, and subsiding in the course of an hour or two. It is necessary to maintain the physiological impression of the drug to insure the best results.*

Dr. J. Milner Fothergill has recently drawn attention to the value of strychnia as a respiratory stimulant in *dyspnœa* dependent upon pulmonic affections, such as chronic *bronchitis*, *emphysema*, and *phthisis*. In long-standing *bronchitis*, or "*winter-cough*," with a dilated right heart, the combination of strychnia and digitalis in his hands has acted exceedingly well. In other cases he is accustomed to add the strychnia to ordinary stimulant cough mixtures.

In *dyspepsia* or *constipation* or *diarrhœa*, connected with atony of the visceral muscular coat, strychnia is a very valuable remedy. In various local paralyses, such as *prolapse of the rectum*, *atonic retention of urine*, *atonic incontinence*, *and loss of voluntary motion* in certain groups of muscles from temporary injury to the supplying nerve or even from so deep-seated a disease as *infantile paralysis*, it is useful. There is reason to believe that it sometimes does good in these cases by influencing the nutrition of the affected muscle or the peripheral nerves; and it should be injected into the affected part.

Toxicology.—Sufficient has already been said in regard to the general symptoms of strychnia-poisoning. It only remains to discuss the diagnosis.† This is especially important, because strychnia is frequently used criminally, and because not rarely it is impossible for the chemist to detect it after death.

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* This paragraph was written by Dr. S. D. Risley, and is expressive of the results at the University Hospital, where he is chief assistant of the Ophthalmological Clinic.

† A lesion found in one case by Moriz Rosenthal may possibly be characteristic. It is numerous small cross-rents in the heart-muscle, accompanied by small extravasations (*Nervenkrankheiten*, 1870, p. 334).

The only disease with which poisoning by it may be readily confounded is tetanus, in its various forms of idiopathic, rheumatic, traumatic, infantile, and hysterical. It has been asserted that in fatal cases the duration of the attack will always distinguish between natural tetanus and that produced by poison. Dr. Louis Starr, however (*Philadelphia Medical Times*, vol. iii. p. 311), reports a case of traumatic tetanus fatal in less than twelve hours after the first appearance of muscular twitchings, and within one hour and a half after the first convulsion; and according to Jaccoud death has occurred fifteen minutes after the reception of the injury (*Pathologie Interne*, i. 441).

The following table shows, I think, in as clear and brief a manner as possible the differences[*] between traumatic or idiopathic tetanus (No. 1), hysterical tetanus (No. 2), and strychnic poisoning (No. 3). The references in column No. 3 are to authorities who affirm that the symptoms there given are peculiar to poisoning.

No. 1.	No. 2.	No. 3.
	Commenced with blindness and weakness.	Begins with exhilaration and restlessness, the special senses being usually much sharpened.[†] Dimness of vision may in some cases be manifested later, after the development of other symptoms; but even then it is rare.
Muscular symptoms usually commence with pain and stiffness of the back of the neck, sometimes with slight muscular twitchings; come on gradually.	Muscular symptoms commenced with rigidity of the neck, which gradually "crept over the body," affecting the extremities last.	Muscular symptoms develop very rapidly, commencing in the extremities, or the convulsion, when the dose is large, seizes the whole body simultaneously.[‡]
Jaw one of the earliest parts affected; rigidly and persistently set.	Jaw rigidly set before a convulsion, and remained so between the paroxysms.	Jaw the last part of the body to be affected: its muscles relax first, and, even when during a severe convulsion it is set, it drops as soon as the latter ceases.[§]
Persistent muscular rigidity, very generally with a greater or less degree of permanent opisthotonos, emprosthotonos, pleurosthotonos, or orthotonos.	Persistent opisthotonos, and intense rigidity between the convulsions; and after the convulsions had ceased the opisthotonos and intense rigidity lasted for hours.	Muscular relaxation (rarely a slight rigidity) between the convulsions, the patient being exhausted and sweating. If recovery occur, the convulsions gradually cease, leaving merely muscular soreness, and sometimes stiffness like that felt after violent exercise.[‖]
Consciousness preserved until near death, as in strychnic poisoning.	Consciousness lost as the second convulsion came on, and lost with every other convulsion, the disturbance of consciousness and motility being simultaneous.	Consciousness always preserved during convulsions, except when the latter become so intense that death is imminent from suffocation, in which case *sometimes* the

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[*] Column No. 2 is from an actual case. See Trial of Mrs. Wharton, *New York Medical Record*, 1873.

[†] Taylor, *On Poisons*, p. 683. Wormley, *Micro-Chemistry of Poisons*, p. 536.

[‡] Wormley, p. 536. Stillé, *Therapeutics*, vol. ii. p. 148.

[§] Taylor, *On Poisons*, pp. 134, 682. Wormley,—pp. 536, 540, 541. Tardieu, *Sur l'Empoisonnement*, p. 924.

[‖] Taylor, *On Poisons*, pp. 134, 136, 682. Wormley, pp. 536, 540, 541. Tardieu, pp. 924, 938, 939. Husemann, *Handbuch der Toxicologie*, p. 168.

No. 1.	No. 2.	No. 3.
		patient becomes insensible from asphyxia;[*] which comes on during the latter part of a convulsion, and is almost a certain pre cursor of death.
Draughts, loud noises, etc., produce convulsions, as in strychnic poisoning.	Desired to be fanned.	The slightest "breath of air" produces a convulsion.[†]
May complain bitterly of pain.	Crying-spells, in which he "sobbed violently," and "cried like a child," alternated with the convulsions.	Patient may scream with pain, or may express great apprehensions, but "crying-spells" would appear to be impossible.
Eyes open, rigidly fixed, during the convulsion.	Eyes closed.	Eyes stretched wide open.[‡]
	The spasms in leg must have been partial, as the feet were crossed and toes inverted, which could not happen if all the muscles were involved, because the muscles of eversion, being very much the stronger, would of necessity overcome the antagonistic muscles, and the feet be everted.	Legs stiffly extended, with feet everted,[§] as the spasms affect all the muscles of the leg.

Death from strychnia in man and other mammals mostly occurs in a convulsion, and under these circumstances is undoubtedly due to asphyxia, caused by the unyielding spasmodically-contracted muscles. In frogs, death must occur from other causes, since a frog, as shown by Claude Bernard, will live for days after removal of its lungs, probably by breathing through its skin. The causes of death in the frog are not hard to find when the physiological action of the drug is known. The lymph and true hearts (Kölliker, *loc. cit.;* Harley, *Lancet*, July, 1856) are very much affected, but the chief factor is no doubt paralysis of the motor nerves. In man, death sometimes occurs not in a paroxysm, but during relaxation, and probably then is the result not only of the exhaustion following effort, but also of the direct action of the poison on the nerves.

The minimum fatal dose of strychnia is probably something under half a grain; the latter quantity has several times produced death, once in a man in twenty minutes (*Guy's Hosp. Rep.*, 1865, vol. xi. p. 208); one-third of a grain given at intervals in fractional doses has produced such alarming symptoms as to indicate that in a single dose it might readily destroy life; the $\frac{1}{100}$ grain is said to have killed a child three and a half months old (*Pharm. Journ. and Trans.*, viii. 1010); but ten grains (Tschepke, *Deutsches Klinik*, 1861), twenty grains (A. E. Connor, *Ohio Med. Recorder*, 1879, 12), also twenty-two grains (Dr. Geo. Gray, *Brit. Med.*, 1880, i. 477) taken on a full stomach and retained two hours, have failed to cause death, in each case probably on account of slow absorption.

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[*] Wormley (1st ed.), p. 536. Taylor, *Medical Jurisprudence*, pp. 331, 332. Wharton and Stillé, *Medical Jurisprudence*, paragraph 757. Tardieu, p. 923. Stillé, *Therapeutics*, p. 148.

[†] Stillé, *Therapeutics*, p. 148.

[‡] Stillé, *Therapeutics*, p. 148. Wormley, p. 536. Tardieu, p. 924.

[§] Tardieu, p. 924; also other authorities, which I have neglected to note, and at present writing have not at hand.

In treating poisoning by strychnia, a chemical antidote should be at once administered, such as tannic acid, or iodine, or one of its soluble salts. As, however, the compounds formed in the stomach by these substances are not permanent, a quick emetic must follow their administration. For the treatment of the symptoms, various substances have been recommended. Aconite, Calabar bean,[*] tobacco, or their alkaloids, would appear to be indicated as physiologically antidotal. The evidence brought forward by Dr. Haughton and others is not sufficient to establish clearly the especial value of tobacco, and in the experiments of M. Amagat (*Journ. de Thérap.*, 1875) nicotia seemed to have no power in preventing the death of rabbits which had received a fatal dose of strychnia. Further, it is obvious that the use of aconite, or of tobacco, in large doses, is accompanied with grave danger, on account of their influence upon the heart, and we have in bromide of potassium a substance devoid of any such objection, and apparently as complete a physiological antidote to strychnia as are any of the substances above named. The chief question is as to whether the bromide has sufficient power and swiftness of action. In Dr. C. L. Bard's case[†] (*Phila. Med. Times*, i.), recovery after the ingestion of three grains of the alkaloid, without vomiting, occurred, under the exhibition of a half-ounce dose of the potassium salt and "its continued use in smaller doses for an hour or so." The symptoms were as intense as was consistent with life, but general relaxation was produced in thirty minutes after the ingestion of the counter-poison.

Chloral was stated by Liebreich, its therapeutic discoverer, to be antagonistic to strychnia, and it undoubtedly is so in a measure; but M. Orr (*Gazette Médicale*, July 6, 1872) stated to the French Academy that he had experimentally proven that the dose of chloral which Liebreich had relied on as being mortal to rabbits was very often not so, that the same was true of strychnia, and that consequently the investigation of Leibreich was not to be relied on as proving the respective antidotal powers of the drugs; and, further, that experiments had shown him that if a certainly-fatal dose of chloral were given to a rabbit, the hypodermic injection of strychnia did not affect the result, but that his own researches had not gone far enough to establish the exact relations of the drugs. Prof. Bennett (*British Med. Jour.*, vol. ii., 1874) has made an elaborate study, which agrees with the experiments of Orr in showing the non-efficiency of strychnia in chloral-poisoning, but also proves that chloral is of great value in poisoning by the alkaloid. Out of twenty-one rabbits which had received much more than the minimum fatal dose of strychnia (gr. $\frac{1}{280}$ to the pound) fifteen were saved by the use of chloral, and a few days later were killed in from ten to twenty minutes by a repetition of the original doses of strychnia. Dr. Bennett found that the chloral administered after the supervention of convulsions had less effect in saving life in direct proportion to the length of time between its administration and that of the poison. Prof. Husemann (*Arch. Exper. Path. und Therap.*, x.) found it possible to prevent death by chloral in rabbits which had received five or even six times the minimum fatal dose of the alkaloid. In various cases recovery from the effects of large doses of strychnine (four grains, *Edinb. Med. Journ.*, April, 1875; six grains, *Arch. Gén. de Méd.*, 1883, i. 74, where also numerous cases may be found) has been brought about by the use of chloral, which must be at present considered a standard remedy in strychnine-poisoning. Alcohol has been strongly recommended by some authorities (Amagat, Stacchini) as antidotal; and when the great muscular relaxation of drunkenness is remembered, it seems very probable that the commendation has some basis. Prof. Husemann (*loc. cit.*) has, however, shown that alcohol can scarcely be looked upon as a real antagonist to the alkaloid.

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[*] Two cases of recovery very doubtfully attributable to Calabar bean, *Ohio Med. Recorder*, iv. 154.

[†] For other successful cases, see *New Remedies*, vol. ii. p. 255; also, *Chicago Med. Examiner*, xxxix., 1879, 280.

The best treatment of strychnia-poisoning is apparently to be found in the conjoint use of chloral and the bromide of potassium, with, when convulsions are very threatening, inhalations of nitrite of amyl, ether, or even chloroform. Half an ounce of the bromide with half a drachm to a drachm of chloral may be given at once in a severe case; and every twenty minutes afterwards, if necessary, two drachms of the first and fifteen grains of the econd remedy.

In some cases, artificial respiration might possibly be of service. It is evident that the convulsed muscles will often resist such efforts as are usually made to force air into the lungs of man as successfully as they do the unassisted struggles of nature; and Harley states that he has found artificial respiration of no use whatever in animals. On the other hand, Leube (*Archives Anat. et Physiol.*, 1867), in an apparently very careful series of experiments, found that artificial respiration has great influence in saving or prolonging life, according to the amount of the poison ingested. In his experiments, the dose which ordinarily produced convulsions did not do this so long as artificial respiration was kept up; and the "lethal dose" did not kill if artificial respiration was maintained for four hours, although opisthotonos was induced in some cases. Jochelsohn only succeeded in prolonging life (*Rossbach's Untersuchungen*, i., 92), but Rosenthal, according to Husemann, obtained similar results to Leube, and M. Schiff (*Schmidt's Jarbücher*, Bd. cxli. p. 43) has, in a series of experiments, corroborated in the main facts the results of the German investigators, although disagreeing with them in minor particulars. He found that animals in which *forcible* artificial respiration was maintained survived doses much larger than those ordinarily fatal. The artificial respiration was performed by inserting a canula into the trachea, and filling the lungs by force. Klapp also found artificial respiration of service. None of the ordinary methods of artificial respiration in man are, however, sufficiently powerful to be of any value.

ADMINISTRATION.—As a tonic, strychnia may be given in pill; but when it is desired to push it until its physiological effects are manifested, as in some cases of *paralysis*, it should be always administered as the sulphate in solution, because death has occurred from an irregularity in the solution of the pills in the alimentary canal and the consequent simultaneous letting loose of a large amount of the alkaloid. There is no proof of a cumulative action of this alkaloid when given as above directed. Dose, one-twentieth of a grain, gradually increased *pro re nata.*

$\frac{1}{60}$ - $\frac{1}{20}$

STRYCHNINÆ SULPHAS. U.S.—*Sulphate of Strychnine* occurs in minute, prismatic crystals. It is soluble in water, and therefore preferable to the alkaloid for hypodermic use. Dose, one-twentieth of a grain.

BRUCINE.—L. Wintzenreid (*Dissert. Inaug.*, Geneva, 1882), in an elaborate investigation, finds that brucine acts as a stimulant to the spinal cord and a paralyzant to the motor nerves, but does not influence the cerebrum or the sensory nerves: in the higher animals, at first it increases the arterial pressure, and afterwards lessens it; paralyzes in large doses the vagi; causes death by asphyxia, and in other ways acts like strychnine.

IGNATIA. U. S.—The seeds of Strychnos Ignatia, a tree growing in the Philippine Islands. The *St. Ignatius Beans* are pale brown, about an inch in length, less in breadth, often angular, with three or four faces, covered with a very fine, scarcely visible down. They have been compared by some to an olive in size and appearance. They contain largely of the igasurates of strychnine and of brucine, and are identical in their therapeutic value with nux vomica. The only officinal preparations are the *abstract* (*Abstractum Ignatiæ*, U. S.), dose, one grain, and the *tincture* (*Tinctura Ignatiæ*—1 to 10, U. S.), dose, twenty minims; the dose of the *extract* (*Extractum Ignatiæ*, U. S. 1870) is one-fourth to one-half a grain.

CLASS X.—DEPRESSO-MOTORS

UNDER this heading are considered certain drugs which are used for the purpose of lessening the activity of the spinal cord. They have, except in this particular, but little in common in their action, and must be studied individually.

PHYSOSTIGMA—CALABAR BEAN. U.S.

An irregular, kidney-shaped bean, about an inch in length and three-fourths of an inch wide; the product of the Physostigma venenosum, a perennial woody creeper of Calabar, Africa, where the bean has been used by the natives as an ordeal test for criminals, witches, etc., since time immemorial. It contains an alkaloid known as *physostigmia*, or *eserina*. The most reliable tests for the alkaloid are as follows. A watery solution of it or of its salts containing potassa, soda, or lime, on exposure to the air, becomes red, and finally yellow, green, or blue: this is said to occur when only one one-hundred-thousandth part of the alkaloid is in the solution. Chloride of gold throws down from the solution a blue precipitate, out of which the gold is soon reduced. According to Dr. J. B. Edwards (*Medical Times and Gazette*, 1864), with strong sulphuric acid and bichromate of potassium physostigmia yields a violet color, passing into red. This point needs investigating, in relation to the well-known strychnia test. The physiological test consists in the placing of a drop of the suspected solution in the eye of a rabbit, when, if physostigmia be present, contraction of the pupil will be produced in from eight to twenty minutes. A second alkaloid, *calabarina*,* has been found by E. Harnack and L. Witkowski (*Arch. Experim. Path. und Pharm.*, Bd. v.), in especial abundance in commercial extracts. As Prof. Harnack has succeeded in producing it from physostigmia (*Ibid.*, Bd. xii.), it is a natural suspicion that it is formed by decomposition of the physostigmia during the preparation of the extract. It is much less soluble in ether than is physostigmia, from which it may be separated by means of that menstruum.

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* Calabarina, according to its discoverers, is a tetanizing agent resembling strychnia in its action upon frogs and other of the lower animals. Prof. Husemann found, however, that Merck's "Calabarinum purum" acts in an entirely dissimilar manner, but Harnack has shown that this commercial article contains little or no calabarina (see *Arch. Exper. Path. und Therap.*, Bd. viii. 125; ix. 434; x. 301). It is possible that physostigmia has a strong tendency to undergo various decompositions, and to produce under different circumstances diverse derivative alkaloids.

Physiological Action.—When an animal receives a small fatal dose of Calabar bean, after a time muscular tremors appear, and almost immediately the animal falls to the ground, or lies down, in a state of perfect muscular flaccidity. The pupils generally contract, and the respirations become slow, irregular, and often stertorous. All reflex actions are almost at once diminished, and this diminution grows greater and greater, until it ends in their complete abolition. So long as the condition of the motor system allows of it, evidences of sensibility are manifested whenever the animal is in any way injured. According to Clementi Papi (*Schmidt's Jahrbücher*, Bd. cxlii. p. 287), the voice is completely lost. The muscular tremors persist during the whole period of paralysis, and, indeed, even after cessation of the respiration. They vary greatly in intensity, and in some cases are so severe (Fraser) as to simulate general convulsions. As the minutes go by, the rhythm of the respirations becomes more and more affected, and at last death takes place quietly, consciousness being preserved until the last few gasping respirations close the scene. The pupils sometimes, but not always, dilate immediately after death. According to the experiments of Dr. Fraser, the bodily temperature is slightly elevated.

After a small lethal dose of the poison, the fatal result is always due to failure of the respiration, and if the body be at once opened the heart is found still beating; indeed, it has been seen to continue to do so for one and a half hours after death (Fraser). If a very large amount of the drug be given, the animal falls almost at once, paralyzed, with only a few muscular twitchings. The pupils contract, and in a very short time the gasping respiration ceases. The heart is now found distended and passive, but often will contract under the stimulation of a galvanic current.

The symptoms induced by the drug in man are completely parallel with those that occur in the lower animals. They are giddiness, lessened heart-action, great muscular weakness, with, in most cases, contraction of the pupil, and sometimes with vomiting, and still more commonly with purging, which may be very free. A pupil of Gubler took 0.15 grain of the sulphate of eserina, and suffered, after a time, nausea, giddiness, and intense muscular weakness, so that he could not stand; three-quarters of an hour afterwards he vomited some of the solution mixed with bile, but his strength did not begin to return for two and a half hours.

These tremors have been seen after so-called pure physostigmia by Rossbach and Fröhlich. Köhler, Rossbach, and others have even affirmed that Calabar bean produces a tetanic intoxication. A plausible explanation of these singular observations, and of many of the discrepancies of authorities, is to be found in the discovery of calabarina. Its discoverers state that it produces first a violent tetanus, and afterwards paralysis. It is plain how its presence in varying amounts in Calabar bean preparations would modify their action. The researches of Köhler, of Vintschgau, and of Rossbach and Fröhlich, are especially open to doubt, on account of their statements that Calabar bean tetanizes. It is very probable the extracts used by them contained largely of calabarina.

The question here naturally arises, To what is the paralysis so prominent in poisoning by Calabar bean due? It is evident that the suspension of reflex action can have only three sources: paralysis of the spinal cord, of the nerve-trunks, or of the muscles. I shall examine the action of the drug upon these organs in inverse order.

Muscles.—The muscular twitchings which have already been spoken of have been mistaken for convulsions by M. Vintschgau (*Sitzungsberichte der Math.-Nat. Classe d. k. Akad. d. Wissenschaften*, Wien, 1867, Bd. lv., Abth. ii., p. 49), who, indeed, concluded that Calabar bean acts like strychnia, because violent convulsive tremors occurred, after injection of a dose of the poison under the skin, in all parts of a frog whose iliacs he had tied. Evidence to be brought forward hereafter, however, shows conclusively that there was some fallacy in this experiment. The fact that the muscular movements continue after death indicates that they are due to a direct action of the drug upon the muscles themselves. This conclusion is thoroughly established by the experiments of Laschkewich (*Virchow's Archiv*, 1866, Bd. xxxv. p. 294), of Fraser (*loc. cit.*), and of Leven and Laborde (*Schmidt's Jahrbücher*, Bd. cxlvi. p. 136). All of these investigators have noted that after death these contractions are increased by exposure to the air and by direct stimulation of the muscles; and Fraser has found that they occur in the frog during life after section of the supplying nerve, and also in a muscle actually cut out of the body. Laschkewich has confirmed the latter fact in the case of warm-blooded animals, and Leven and Laborde have proven that previous destruction of the lower end of the spinal cord in a guinea-pig does not prevent the development of the muscular twitchings in the hind legs. Although Calabar bean does, therefore, have some direct influence upon the muscles, yet the paralysis produced by it is in no sense the result of this influence, which appears, indeed, to be of an exciting rather than of a paralyzing character, since at the time of death the contractility of the muscle is in no wise diminished: on the contrary, Fraser has noted that in poisoning by Calabar bean the supervention of rigor mortis and of loss of functional power in the muscle is very greatly delayed.

Nerves.—The paralysis caused by the physostigma is not due to an action on the nerve-trunks, since Dr. Laschkewich, Dr. Vintschgau (*loc. cit.*, p. 161), and also Dr. Fraser, have found that when the galvanic current is applied to the crural nerve of either cold- or warm-blooded animals rapidly killed with Calabar bean, contractions are freely induced in the tributary muscles.

Indeed, the Scotch investigator, carrying his experiments still further, and using delicate instruments which it is not necessary here to describe, discovered that when the artery going to a hind leg was tied in a frog before the administration of the poison, after a *quick* death the rate of conduction of impulse was as rapid in the nerve to which the poison had had free access, as in its protected fellow. Notwithstanding these facts, the drug is not entirely without influence upon the nerves, since Dr. Fraser has found that when the blood-vessels of a frog's leg are tied, and the animal slowly poisoned by a small dose of the extract, whilst even many minutes after cessation of respiration both nerves seem equally intact, yet finally a time comes when the nerve of the poisoned leg refuses to react to the galvanic stimulus, although the functional power of the protected nerve, as well as of the muscles, is still perfect. This loss of functional power is probably rather in the termination of the nerve than in the trunk, for Dr. Fraser found that when all the blood-vessels supplying the gastrocnemius muscle were cut in a frog and the animal poisoned, at a certain time irritation of the crural nerve produced spasms of the gastrocnemius alone. It is to be noted that this perturbation of the peripheral nerves has only been seen in the frog when slowly poisoned, in which case the heart continues to beat long after the cessation of respiration, so that the nerves are, as it were, macerated in a solution of the poison. Its existence, even in this feeble degree, is denied by Harnack and Witkowski. In frogs, and still more in warm-blooded animals, nerve-paralysis, if it exist at all, is of such slight intensity as to be of no practical importance.

The afferent nerve-fibres probably preserve their function after the motor fibres have been affected, as was seemingly proven in Dr. Fraser's experiments (*loc. cit.*, p. 19) by tying the vessels in the left leg of a frog which was afterwards poisoned with strychnia, when it was found that reflex movements were excited in the left leg by irritation of the right foot long after irritation of the left foot had ceased to cause movements in the right leg.

Dr. Fraser studied to some extent the effect of a strong solution of the poison when applied locally to a nerve, and found that the efferent fibres were affected before the afferent, and that finally the function of both of them was abolished.

Spinal Cord.—Since the abolition of reflex activity has its origin neither in the muscular system nor in the nerve-trunks, it must be spinal. The truth of this conclusion, arrived at by exclusion, has been abundantly demonstrated by direct experiment. Thus, Fraser, Harnack, Witkowski, and others have found that if in the frog a peripheral nerve be protected by tying its artery and the batrachian be poisoned with Calabar bean, the paralysis in the protected limb occurs *pari passu* with that in the remainder of the body. Again, Fraser divided the spinal cord of a frog, and then cut or tied all the blood-vessels going to the posterior section of it. After this, the animal was poisoned with physostigma, and, whilst the usual symptoms developed themselves in the anterior portion of the body, reflex actions were unaffected in the posterior part. Further, Dr. Fraser has found that when the poison is applied directly to the cord, fibrillary contractions, due probably to a local irritant influence, are induced in the muscles supplied from below the point of application; but in a little while all movements cease, and even galvanization of the cord is itself unable to elicit response. It seems completely established by the evidence which has been brought forward that the most prominent effect of Calabar bean is a *depressant action upon the spinal centres.*

Recently, however, it has been asserted by Papi (*Schmidt's Jahrbücher*, Bd. cxlii. p. 287) that there is in frogs, preceding the stage of depression, one of exaltation of reflex action; and also, on the strength of some experiments upon animals with one-sided section of the optic thalamus, that the cause of loss of voluntary movement in Calabar bean poisoning is paralysis of the conducting fibres passing from the upper brain to the spinal centres. I have not been able to procure the original paper of Dr. Papi (*Gazz. Lomb.*, 1868), but his conclusions seem to me highly improbable. The primary stage of reflex activity probably was produced by calabarina present in the extract used by him.

Circulation.—Harley (*loc. cit.*, p. 151) and Papi (*loc. cit.*, p. 287) assert that Calabar bean has little or no influence upon the heart; but they are undoubtedly in error. According to Harnack and Witkowski, in the frog under the influence of the poison the heart's contractions become slower and stronger. When a mammal is poisoned with small doses, the cardiac action of the drug is subordinate to that upon the nerve-centres; but, as has been shown by Dr. Fraser, when very large doses of the poison are administered, especially if they be injected into the jugular vein, death results from syncope or from consentaneous failure of the cardiac and the respiratory function, and the heart is found arrested in diastole, flaccid, but, according to Dr. Fraser and to Drs. C. Arnstein and P. Sustschinsky (*Untersuch. Physiolog. Labor. Würzburg*, zweiter Theil, p. 86), responding, though feebly and uncertainly, to direct stimulation. In the frog, Rossbach and Fröhlich (*Pharmak. Untersuch.* i., p. 56) have found that the arrested heart is insensible to stimuli.

When smaller doses of the poison are exhibited, there is slowing of the heart's action, as has been noted by Laschkewich (*loc. cit.*, p. 298), by Fraser (*loc. cit.*, p. 48), by Dr. J. Tachau (*Archiv der Heilkunde*, 1865, p. 70), and by other observers. Although, according to the experiments of Fraser, there is at first a slight fall of the blood-pressure, probably due, as he believes, to diminished pulse-frequency, yet, in spite of the latter, the arterial tension soon recovers itself, and remains for a long time much above the normal point, while at the same time the individual cardiac beats are greatly increased in strength (Fraser, Bezold and Götz*). Finally, the arterial pressure falls far below normal, and the power of the heart is gradually extinguished.

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* I have not seen the original paper of these authorities in the *Centralblatt für Med. Wissenschaft*, 1867, but quote them from the paper of Arnstein and Sustschinsky.

The question as to the exact method in which these changes are wrought is of very difficult answer. The long diastolic pauses and the slow strong beat of the heart suggest at once that a chief action of the drug is upon the inhibitory cardiac nervous system. Tachau, however (*loc. cit.*, p. 172), found that after section of the vagi the poison produces these phenomena in an even more intense degree than in the normal heart. As this has been confirmed by Laschkewich (*loc. cit.*), by Fraser (*loc. cit.*, p. 49), and by Harnack and Witkowski (*loc. cit.*, p. 419), it must be accepted as a proven fact, especially since Vintschgau has found (*loc. cit.*, p. 71) that if in the frog the brain and the medulla be destroyed, physostigmia still acts in its usual way on the heart.* Tachau considers that this demonstrates that the cardiac phenomena of Calabar bean poisoning are not due to an action of the drug upon the inhibitory nerves. Arnstein and Sustschinsky, however, admitting the fact, deny that it warrants the conclusion. Their idea appears to be that it is conceivable that a substance should so act upon the peripheral inhibitory nerve-endings as to cause them to influence the action of the heart without any external impulse, and consequently when separated from the nerve-centres. With our present knowledge, the possibility of this seems somewhat doubtful. Moreover, Köhler, Harnack, and Witkowski have all found that in the frog Calabar bean still lessens the pulse-rate after complete paralysis of the peripheral vagi by atropia† (*Archiv f. Exper. Path. und Pharm.*, Bd. i. p. 280). Köhler believes that his experiments prove that the Calabar bean paralyzes the cardiac accelerator nerves. It will be remembered, however, that Vintschgau found that Calabar bean exerts its normal influence upon the heart after destruction of the accelerator centres. Whatever may be the action of small doses of physostigmia upon the vagi and accelerators, it seems to me that it must be considered established that the general cardiac symptoms are due to a direct action upon the heart-muscle or its contained ganglia, and that any increase of the inhibitory activity must be of such slight amount as to be of no importance.

In regard to the action of the drug upon the peripheral vagi, the following *résumé* of the evidence is of interest. Arnstein and Sustschinsky found that the excitability of the peripheral cardiac vagi is increased by Calabar bean. They first tested the effect of graduated galvanic currents applied to the divided vagi in the animal to be experimented with, until the exact strength of the weakest current capable of causing diastolic arrest was demonstrated, and then exhibited the drug and tested the nerves afterwards. They used in these experiments both rabbits and guinea-pigs, and found that, without a single exception, currents much weaker than those which previously were barely effective would, after the poisoning, stop the heart; also, the super-excitability of the peripheral inhibitory nerves was shown by the fact that under the influence of the drug the diastolic arrest continued much longer than normal after the withdrawal of the stimulus from the vagi. These experiments have been directly corroborated by Rossbach and Fröhlich upon the rabbit (*loc. cit.*, p. 57). Dr. Fraser's experiments upon the local cardiac application of the drug are also seemingly confirmative of those of Arnstein and Sustschinsky, for he found that when the poison was put directly on the heart, or into one of its chambers, it caused a prolonged diastolic pause, followed by contractions, interrupted by pauses, and finally resumption of regular contractions, or else by diastolic arrest, the heart still retaining its power of responding, in an embarrassed manner, to stimuli. These experiments certainly seem to prove that Calabar bean does cause excitation of the peripheral cardiac apparatus. Arnstein and Sustschinsky further confirm them by other experiments of exceeding interest. They injected into rabbits such amounts of atropia as completely to paralyze the peripheral cardiac vagi, so that the strongest currents when applied to the nerves failed to influence the heart's action, and then *restored functional power* to the pneumogastrics by injections of Calabar bean, so that currents of moderate intensity caused diastolic arrest. These experiments, if accurate, prove that physostigma is a powerful excitant of the peripheral vagi. Köhler (*loc. cit.*), using the frog, and Rossbach and Fröhlich, using the rabbit, failed to resuscitate the atropinized vagi by means of Calabar bean, but it is evident that a negative result in such a case might be due to an improper proportion in the doses of the counter-poison, or in the atropia being employed in overwhelming amount. In warm-blooded animals, at least, the vagi are not paralyzed during life by physostigmia, as is evinced by the experiments of Arnstein and Sustschinsky (*loc. cit.*, p. 101), confirmed by Harnack and Witkowski (*loc. cit.*, p. 433). Some of the results obtained by Fraser (*loc. cit.*, p. 36), confirmed by Rossbach and Frölich, apparently contradict, but in reality accord with them. In the frog there was, indeed, at last a loss of functional power in the vagi, but not until very long after the cessation of respiration, after all the nerves of voluntary motion had lost their functional power,—*i.e.*, after death would have occurred in a mammal. Harnack and Witkowski affirm that the vagi never lose their power in the frog to lessen the rate of the heart-beat, although unable to cause diastolic arrest.

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* The fact that Calabar bean acts in its usual manner after section of the par vagum indicates that it has no influence upon the inhibitory centres,—a conclusion confirmed by Arnstein and Sustschinsky (*loc. cit.*, p. 102), who found that an injection of the drug into a carotid—*i.e.*, into the inhibitory centre—did not cause any marked immediate diminution in the number of the cardiac pulsations.

† Rossbach and Fröhlich (*loc. cit.*, p. 56) assert that in frogs, although the vagi are not more excitable before than after the poisoning, stimulation of the venous sinuses and of the auricles has much more than the normal influence, which is very extraordinary if true.

In summing up the evidence in regard to action of the drug upon the vagi, it is plain that no positive conclusion can be reached, although it seems probable that the drug first increases and then lessens the power of the inhibitory nerves over the heart.

As already stated, a very prominent phenomenon in Calabar bean poisoning is rise of the arterial pressure. This, of course, may be of cardiac origin, or it may be due simply to a contraction of the arterioles; or it may arise from a combination of these causes. Bezold and Götz (quoted by Arnstein and Sustschinsky, p. 87) found that the arterial pressure still rose under the influence of the drug after section of the spinal cord high up,—*i.e.*, after general vaso-motor paralysis. Harnack and Witkowski also found that when the vaso-motor centres were paralyzed with chloral, physostigmia causes very decided increase of the arterial pressure. It is evident the increased force of the circulation produced by physostigmia must, at least in part, be due to a direct action of the drug on the heart.

The fact that the rise of arterial pressure produced by Calabar bean is not so great in animals whose cords have been divided as in those uninjured certainly indicates, though it does not prove, that the increased arterial tension of physostigmia-poisoning is in part due to *vaso-motor spasm.* Dr. Fraser believes that Calabar bean does produce this spasm; but his evidence is insufficient to establish his conclusion. It consists simply of some experiments upon frogs in which the spinal cord was divided, and, the animal being put on a "frog-plate," the arteries of the web were watched whilst Calabar bean was exhibited. Dr. Fraser believed that under these circumstances the arteries contracted considerably at first, and afterwards dilated. Dr. Harley (*Practitioner*, 1869, vol. iii. p. 163) states as the result of his studies that Calabar bean can be seen, when applied locally, to cause contraction of the veins, the arteries remaining unaffected; whilst Fraser, in contradiction to this, believes that he has demonstrated that the local application of physostigma produces dilatation of the arteries. It is not necessary here to reiterate my objections to such evidence as this. If, under the circumstances of the first-mentioned experiments of Dr. Fraser, Calabar bean contracts the small vessels, it must be by a peripheric, not centric, action, since the vessels were separated by the division of the cord from the vaso-motor centres. It is plain that this is in direct contradiction to Dr. Fraser's experiments on the local application of the drug. Again, it is contradictory, rather than confirmatory, of that furnished by the study of the blood-pressure. The only logical conclusion seems to me to be that at present we have not proof that Calabar bean acts upon the vaso-motor nervous system. As the increase of the arterial pressure is in great part, if not altogether, due to the increased energy put forth by the heart under the influence of physostigmia, and as that influence is exerted directly upon the heart-muscle or its ganglia, it is evident that physostigmia directly causes the heart to put forth more effort, or, in other words, stimulates it. The final diastolic arrest (the loss of the power of responding to stimuli) shows, however, that at last the poison paralyzes the heart. In considering the general physiological action of the drug, it must not be forgotten that its influence upon the heart is entirely subservient to its influence on the nervous system,* and that death in the mammal occurs before the stage of cardiac palsy is reached, unless the drug be injected directly into the heart in overwhelming dose.

I do not believe that physostigma has much action upon the *blood*. Certainly its influence upon the nervous system is a direct one, since Lewisson (*Reichert's Archiv*, 1870) has found that it acts upon the "salt frog" as upon the normal animal. Fraser, however, states that after death from this poison the blood coagulates slowly and loosely, and the red disks in dogs and in rabbits present various irregularities of outline, among which may be noted a well-marked stellar crenation, but that the respiratory function of the blood is not interfered with.

Intestines.—Intestinal peristalsis is very much increased by the action of Calabar bean (Westermann, *Schmidt's Jahrbücher*, Bd. cxxxviii. p. 290; Papi, *Ibid.*, Bd. cxlii. p. 287; Fraser, *loc. cit.*, p. 57). After poisonous doses there is at first a stage of exceedingly active movements in the bowels; then spasmodic tetanic contraction of the intestines occurs, so that their calibre is very much diminished; and finally relaxation and dilatation take place. After death the vermicular movements are found very much lessened (Fraser), or altogether abolished (Tachau, *loc. cit.*, p. 73).

The action of Calabar bean upon the intestines appears to be peripheral, due to contact of the poison in the blood with the muscular fibres or the ganglionic nerve-cells in the walls of the bowels. For Westermann (*loc. cit.*, p. 291) found that extirpation of the cardiac ganglion had no effect upon the action of the drug, but that tying of the mesenteric and of the cœliac arteries, before poisoning, prevented any increase in the peristalsis. Calabar bean probably influences intestinal secretion. Its action upon the salivary glands is often decided, and according to Heidenhain is not prevented by atropia.

Eye.—Calabar bean, as is well known, strongly contracts the pupil, both when applied to the eye and when exhibited internally. Evidently, as in the case of atropia, the pupillary action of Calabar bean should be studied from two points of view, the local and the constitutional.

The closeness of the analogy between the pupillary action of atropia and that of Calabar bean is seen in the fact that, like the former, the latter, as shown by the experiments of Vée and Leven on chickens (*Comptes-Rendus de la Société de Biologie*, 1865, p. 161), does not affect the irides of birds. Thus, analogy would seem to prove that the influence of Calabar bean is directly upon the peripheral nerves of the iris.

Although, then, I am not able to cite any direct experimental proof, yet it seems to me scarcely doubtful that the contraction of the pupil produced by Calabar bean is always a local, peripheral influence, whether the drug be placed in the eye from the outside or be carried to the general circulation. It is evident that the myosis may be caused in one of three methods: by paralysis of the sympathetic fibres, by stimulation of the oculo-motor fibres, or by a conjoint action upon both sets of nerve-endings. In which of these ways the drug acts, we are not yet able to decide.

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* For a discussion of the peculiar cardiac relations of physostigmia and muscarin, see the paper by Harnack and Witkowski. Those authors believe that Calabar bean sets in motion the heart arrested in diastole, not by paralyzing the cardiac inhibitory apparatus, but by stimulating the cardiac muscle.

It has been held by various authorities that if galvanization of the sympathetic fibres in the neck fail to expand a contracted pupil, the myosis must be due to paralysis of the sympathetic. Evidently, however, this is claiming too much, for, as pointed out by Grünhagen (*Virchow's Archiv*, Bd. xxx. p. 521), it is conceivable that an oculo-motor spasm can exist of such intensity that the antagonistic nerve is unable to dilate the pupil. The question arises very pertinently at this point, What is the fact in regard to Calabar-myosis? Does or does not galvanic stimulation of the cervical sympathetic dilate the pupil? The testimony is somewhat conflicting. Dr. Grünhagen (*loc. cit.*, p. 521) says that dilatation always occurs, although to a slight extent (*in beschränkten Masse*); whilst, on the other hand, Dr. Gustav Engelhardt (*Untersuchungen aus dem Physiologischen Laboratorium in Würzburg*, zweiter Theil, p. 526) has found that galvanization of the cervical sympathetic has no effect upon the contracted pupil. The experiments of Fraser (*loc. cit.*, p. 60), of Bernstein and Dogiel, and of Rosenthal (*Reichert's Archiv*, 1863), would seem to reconcile these differences, and by their accord, to prove that under the maximum influence of Calabar bean the sympathetic is powerless, whilst when the contraction is the result of a milder influence of the drug, stimulation of the cervical nerve will cause a certain amount of dilatation.* Fraser, and also Engelhardt, have found that if the poles of a battery be applied directly to an iris even most profoundly contracted by physostigma, immediate dilatation occurs. These facts, for reasons stated above, do not absolutely prove, but they certainly render it highly probable, that Calabar bean *paralyzes the peripheral sympathetic nerve-fibres* in the iris. It is, however, almost equally probable that there is a consentaneous *stimulation of the oculo-motor* terminations; for the myosis caused, like the mydriasis produced by atropia, is an active, not a passive, condition, and is not only much more forcible, but is also much more complete, than that which follows section of the cervical sympathetics. If the observation of Rossbach and Fröhlich be correct, that overwhelming doses of the physostigmia finally dilate the pupil, it is evident that the oculo-motor stimulation is replaced after such doses by oculo-motor palsy.

Urine and Elimination.—No study, that I am aware of, has been made either as to the elimination of Calabar bean or its action on the urinary secretion in health. Dr. Merson (*Journal of Mental Sci.*, Jan. 1875) has found that in general paralysis under its influence urea and the other solids of the urine are decidedly diminished. The physostigma probably escapes with the renal secretion, and in a case of poisoning its presence could probably be detected by dropping some of the fluid in the eye of an animal.

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* Recently Rossbach and Fröhlich affirmed that galvanization of the sympathetic still causes dilatation, even when the action of the physostigmia is most vigorous. As it is scarcely conceivable that the various other investigators should have been so much in error, it is probable that Rossbach and Fröhlich used such strong currents that they were directly transmitted to the iris.

THERAPEUTICS.—The physiological action of Calabar bean has suggested its use in spasmodic affections, in atony of the muscular coats of the bowel, and in various diseases of the eye.

The action of Calabar bean upon the spinal cord very early led to its use in spasmodic affections, and especially in *tetanus*, in which disease it has been more freely employed during the last few years than any other remedy except opium. In the paper of Dr. B. Roemer (*St. Louis Medical and Surgical Journal*, 1873, p. 367) are collected forty-seven cases, of which twenty proved fatal. To these I am able to add the twenty whose references are given below,[*] making in all sixty-seven cases, with thirty-seven recoveries and thirty deaths,—not a very flattering record.

It is, however, proper to state, as affecting the value of these statistics that much of the Calabar bean extract which has been offered in the market is practically inert, and in all probability in some of these cases the drug did not have a fair trial; and that when especial care was taken by certain observers better results were achieved, although on so small a scale as to leave the issue in much doubt.[†]

In *trismus neonatorum*, Calabar bean has been employed with results certainly no more encouraging than those obtained in tetanus. In *chorea* it has also been used by some practitioners with asserted advantage, but further experience hardly justifies its administration (see *Bull. Gén. Thérap.*, lxxxix., 85, 541).

The physiological action of physostigma upon the unstriped intestinal muscle-fibres has led to its employment in *atony* of the muscular coat of the bowels and other similar organs. Dr. V. Subbotin (*Archiv f. Klin. Med.*, Bd. v. p. 285, 1869) has used the extract with the happiest results in a case of *chronic bronchial catarrh* with intense *dyspnœa*, believed to be due to weakness of the bronchial muscular fibres; and also in one of apparently "*phantom tumor*," with *chronic intestinal dyspepsia* and *catarrh*. In *constipation* dependent upon relaxation, it is also said to be useful. Dr. A. Hiller also strongly endorses the value of the extract in *chronic intestinal atony*, after or during a catarrh, in the convalescence from fever, etc., and in *constipation* with flatulence, in meteorism, etc. (*Charité Annalen*, 1883, 235).

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[*] FATAL CASES.—Fenwick, 1 (*Glasgow Medical Journal*, 1869, p. 300); Franzolin, 1 (*The Doctor*, Oct. 1, 1871); Laborde, 1 (*British Medical Journal*, June, 1872): Valdivieso, 1 (*Philadelphia Medical Times*, vol. i. p. 455); Tyson, 1 (*Ibid.*, p. 418); Johnson, 1 (*Ibid.*, p. 372); 1 (*London Lancet*, 1874); Silbermann, 1 (*Charier's Thesis*, 1881); Delamarre, 1 (*Paris Thesis*, 1875); Richelot, 1 (*Thèse de Concours*, 1875). RECOVERIES.—Fenwick, 1 (*Glasgow Medical Journal*, 1869, p. 300); Newman, 1 (*Medical Examiner*, July, 1869); W. W. Keen, 1 (*Philadelphia Medical Times*, vol. i. p. 195); J. H. Packard, 1 (*Ibid.*, p. 138); Cunningham, 1 (*British Medical Journal*, i., 1874); 1 (*Cincinnati Lancet*, Sept. 1878). All these cases were of the traumatic form of the disease. Charier, 1 (*Paris Thesis*, 1881); Burnam, 1 (*Lancet*, Jan. 1881); Pooley, 1 (*New York Med. Journ.*, Sept. 1878); Silbermann, 1 (*Charier's Thesis*, 1881).

[†] For a favorable record, see Watson, *Glasgow Medical Journal*, N. S., 1869, vol. i. p. 54; consult also *London Practitioner*, Sept. 1869.

Calabar bean has also been employed in *strychnia-poisoning*, and a recovery obtained after the ingestion of three grains of the latter alkaloid is reported by Dr. J. W. Keyworth (*Glasgow Medical Journal*, N. S., 1869, i. 54).*

In *epilepsy*, some trials have been made of the drug, but its value is very doubtful. Drs. Harnack and Witkowski have found that in epileptic guinea-pigs physostigmia causes a succession of fits lasting for hours and days. They have further noted a similar influence upon man. Recently attention has been called to the employment of Calabar bean as a *galactogogue*, the extract being applied to the breast itself (*Brit. Med. Journ.*, ii., 1876, p. 554).

ADMINISTRATION.—Calabar bean is usually administered as an *extract* (*Extractum Physostigmatis*, U. S.), the commencing dose of which is one-tenth to one-fifth of a grain. The dose of the *tincture* (*Tinctura Physostigmatis*, U. S.) is twenty to forty minims. The alkaloid is preferable on account of its certainty, but care is requisite not to use it too freely. Bouchut has found that in children one-twentieth of a grain, given hypodermically, will produce very decided symptoms, which entirely pass off in about three hours. It is probable that one-fifteenth of a grain, repeated every three hours, will be found to be a moderate dose for the adult. It should always be borne in mind that, in tetanus and other severe diseases, it is necessary to augment the dose until an effect is produced. Harnack gives the minimum fatal dose of escrina as for dogs four to five, rabbits three, cats two to three milligrammes. The frog resists these doses successfully.

TOXICOLOGY.—So far as I know, Calabar bean has not been used, either in Europe or in this country, with criminal intent. In Liverpool seventy children were accidentally poisoned at one time (*Medical Times and Gazette*, Oct. 1864, p. 406). Many of the victims vomited spontaneously, and thus relieved themselves. Those brought to the hospital were in a state of extreme prostration and muscular relaxation. They appeared to suffer almost no pain, only some of them saying they had a little "belly-ache." Among some thirteen examined, only one had the pupils contracted. The only child who did not recover was excessively weak, and, crying out suddenly, was dead of sudden syncope. The heart was found relaxed and flabby, both sides equally full of blood. In the case of a strong man, who had eaten half a bean (*St. Barthol. Hosp. Rep.*, 1879, xv.), the symptoms were great muscular weakness, tightness across the chest, temperature of 96.6° F., very slow, intermittent, irregular pulse, collapse, without vomiting, purging, contraction of the pupils, or abdominal pain.

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* The subject of the asserted antagonism between chloral and Calabar bean will be studied in the article on chloral.

In 1864 Dr. Kleinwächter treated a case of poisoning by an unknown quantity of atropia with Calabar bean, apparently with great benefit. Dr. Bourneville detailed in 1867 some experiments which seemed to show that there is a real antagonism between Calabar bean and the mydriatic, and in 1870 (*Revue Photographique des Hôpitaux*) published five experiments upon guinea-pigs, which were very decisive in that a proven fatal dose of physostigma was given in each case and recovery obtained by the use of non-lethal doses of atropia. In 1869 Prof. Roberts Bartholow, of Cincinnati, on the strength of a few really indecisive experiments, arrived at a conclusion opposite to that of Bourneville. Recently, Dr. Fraser, of Edinburgh, has investigated the subject in so thorough a manner that his essay may serve as a model for those who are desirous of studying questions of antagonisms between poisons. His experiments, three hundred and thirty-one in number, were made chiefly upon rabbits, a few having been upon dogs. He first investigated as to the minimum fatal dose, per pound of the animal, of the preparations used,—the extract of the bean, and the sulphate of eserina. It was ascertained that the minimum lethal dose for rabbits of the extract of physostigma which he employed was 0.4 grain per pound; of the sulphate of eserina, 0.04 grain per pound. Then in sixteen experiments in which recovery followed the administration of a dose of atropia given in combination with a dose of physostigma equal to or in excess of the minimum fatal dose, the animal used was killed long afterwards by a dose of the Calabar bean less than or equal to that from which recovery had occurred under the influence of atropia. In this way a *perfect* demonstration of the power of the counter-poison was obtained.

It was found that the counter-poison acted most efficiently when thrown directly into the veins. Thus, a rabbit weighing three pounds and two ounces received 1.6 grains of the extract, and five minutes afterwards 0.02 grain of atropia, in a vein, and recovery took place; eight days after this, 1.3 grains of the extract killed the same rabbit in nineteen minutes: in another animal which nine days before had been saved from death after the exhibition of 2 grains of the extract by 0.5 grain of the sulphate of atropia, 1 grain of the extract proved fatal in thirteen minutes.

The next series of experiments was undertaken to ascertain the maximum dose of physostigma that can be successfully antagonized by atropia, and the dose in which the latter should be employed. In all cases the atropia was given five minutes before the Calabar bean. It was found that one-fiftieth of a grain of the mydriatic would successfully antagonize one and a half times, but not twice, the minimum fatal dose of the myotic.

One-fortieth of a grain of the atropia was successful against two to two and a half times the minimum lethal dose of physostigma; three-fiftieths was sufficient for three times the minimum fatal dose. The small size of the required doses of atropia is very noticeable, and at the present point in the investigation a very curious result was obtained. It was found that when three times the minimum fatal dose of the Calabar bean was exhibited, the successful dose of atropia ranged from three-fiftieths of a grain to one grain and a fifth. When three and a half times the fatal dose of the physostigma was exhibited, success was achieved only with doses of atropia of from one-tenth to one-fifth of a grain. Unfortunately, there are only seven experiments bearing upon this point; yet its general accuracy, I think, can scarcely be questioned. When a rabbit received four times the lethal dose of physostigma, the mydriatic was powerless.

In the final series of experiments, the atropia was administered five minutes after the physostigma, and it was found that the largest dose of the latter which could be combated successfully was three times the minimum fatal dose, and the range of the dose of atropia was much less than when it was given before the poisoning. Thus, with three times the minimum lethal dose of the Calabar bean, death occurred when three-twentieths or one-fifth of a grain of the antidote was given, but recovery followed the administration of four-twenty-fifths of a grain.

No experiments were made to test the value of physostigma in atropia-poisoning. Dr. Fraser states, however, on what grounds I do not know, that the minimum fatal dose of atropia is twenty-one grains; and he found that when one-half the minimum lethal dose of physostigma is given, together with nine and four-fifths grains, or more, of atropia, death results.

These experiments of Fraser have been in some degree confirmed by the imperfect researches of Amagat (*Journ. de Thérap.*, 1876). Considerations previously given, however, show that the cardiac antagonism of atropia and physostigma must be considered doubtful, and, if it exist, is of little importance. Whatever of life-saving power the mydriatic has in Calabar bean poisoning is evidently dependent upon its stimulant action on the respiratory centres.

The question naturally arises, How far are the results of these experiments applicable to the treatment of Calabar bean poisoning in man? Without discussing this at length, I think the following deductions are obvious: first, that atropia ought by all means to be tried in poisoning by physostigma; second, that the doses of it should never be very large, not exceeding in all the tenth of a grain. The use of atropia should, of course, not cause neglect of such measures of relief as evacuation of the stomach, the external application of dry heat, etc., usual in poisoning by sedative narcotics. Artificial respiration should, when necessary, be assiduously practiced, since death undoubtedly is due to failure of the breathing, and Harnack and Witkowski have found that animals survive very large doses of the poison, when respiration is maintained artificially.

POTASSI BROMIDUM—BROMIDE OF POTASSIUM. U.S.

The bromide of potassium is prepared, according to the officinal method, by precipitating freshly-made solution of the bromide of iron by the pure carbonate of potassium, filtering, and evaporating the resultant solution. It occurs in milk-white cubic or quadrangularly prismatic crystals of an acrid saline taste, freely soluble in water and slightly so in alcohol. When it is mixed with starch, and chlorine is added, a yellow color is developed. A bluish tint betrays contamination with an iodide.

Physiological Action.—*Local Action.*—When a solution of the bromide is applied locally to the heart, it produces instantly marked lessening of its action, and, if in sufficient amount and concentration, even instantaneous diastolic arrest (*Virchow's Archiv*, xli. 101). Upon the voluntary muscles it acts in a similar manner when similarly applied. If its solution be not too concentrated or abundant, however, the muscle of the frog is first thrown into a tetanic spasm (*Dublin Journal*, xlvii. 325); and Dr. Purser suggests that the tetanic symptoms seen in the frog poisoned by the bromide of potassium are due to this action on the muscles. On the nerve-trunks, and also on the nerve-centres, the bromide acts, when applied locally, as a paralyzing poison (*Bull. Thérap.*, lxxiii. 253, 290; also Dr. Amory, *The Physiological and Therapeutical Action of the Bromide of Potassium*, Boston, 1872, Part II., p. 147; also Ringer and Morshead (*Journ. Anat.*, xii. 71). It is, therefore, evident that the bromide of potassium in sufficient quantity is a deadly poison to all the higher animal tissues. In general poisoning of animals by hypodermic injection of the bromide, this local action is often very manifest, and paralysis of the part into which the solution has been thrown follows very rapidly upon the injection. In the form of powder it is affirmed to be somewhat caustic, and has been highly recommended for the destruction of excessive granulations, etc. (*Brit. Med. Journ.*, ii., 1876, 496).

General Action.—Bromide of potassium administered to frogs in minute doses produces as a first result a tetanoid condition, in which there may be very marked opisthotonos. After a short time this stage of muscular excitement gives way to one of great muscular relaxation, and total abolition of reflex actions. Voluntary movements, however, often occur during this period, and the frog which has been lying limp and apparently dead will startle the observer by a sudden vigorous leap. This fact has been so frequently witnessed that there can be no doubt of its truth. It is vouched for by the following observers: J. M. Purser (*Dublin Journal of Med. Sci.*, xlvii. 324, 1869); Lewisky aus Kazan (*Virchow's Archiv*, Bd. xlv. p. 191, 1869); J. V. Laborde (*Archives de Physiol. Norm. et Pathol.*, t. i. p. 423, 1868, and *Comptes-Rendus*, t. lxv., 1867); MM. Damourette and Pelvette (*Bull. Thérap.*, 1867, lxxiii. 249). Very early in the paralytic stage the respiratory movements are affected, and they gradually grow less until their final arrest. When a very large dose of the bromide is given, death may be induced by paralysis of the heart (Albert Eulenberg and Paul Guttmann, *Virchow's Archiv*, xli., 1867); but after a small toxic dose this viscus continues to beat long after the cessation of breathing. If the drug be given by an injection practiced in the vicinity of the heart, sudden cardiac arrest always occurs.

Upon mammals (*Bulletin Thérapeutique*, lxxiii. 256; *Virchow's Archiv*, xli. 97) the bromide acts very much as upon frogs, inducing progressive paralysis, depression of temperature, and death by asphyxia when given in small poisonous doses, and great disturbance of the circulation, with finally diastolic arrest of the heart, when very freely administered.

No case of acute poisoning in man with the bromide of potassium has been recorded. The nearest approach to a toxic effect I have knowledge of was in a medical student at the University, who took an ounce by mistake; he reported that the only effects were immediate severe pain in stomach and œsophagus, nausea, a little vomiting, great thirst, a feeling of weight in the head, and great sleepiness, which lasted for three days.

The results of the continuous employment of large doses of the bromide, however, demonstrate that it acts upon man as upon the lower animals. When it is taken with sufficient freedom to accumulate in the system, a conjunction of phenomena known as *bromism* arises. The cerebral symptoms are a sense of mental weakness, heaviness of intellect, failure of memory, partial aphasia, great somnolence, and depression of spirits. With these there may be decided impairment of the sensibility of the mucous membranes and of the skin, so that titillation of the fauces may be without effect, and, according to Puche, even heat applied to the skin calls forth no complaint: Huette (*Mémoires de la Soc. Biolog.*, 1850) has seen in some cases absolute anæsthesia of the sclerotic conjunctiva. The sexual function is abolished. There is also very generally fetid breath, and an eruption of acne, which may indeed be very severe. Of course, in any individual case of bromism many of these symptoms may be wanting; but when the use of the remedy is persisted in, they all at last become developed in an intense degree. Prof. Edward H. Clarke thus speaks of a case which came under his notice: "The fetid breath becomes nauseous; œdema supervenes on congestion of the uvula and fauces; the whispering voice sinks into aphonia; sexual weakness degenerates into impotence; muscular weakness becomes complete paralysis; reflex, general, and special sensations disappear; the ears do not hear, nor the eyes see, nor the tongue taste; the expression of hebetude becomes first that of imbecility, then that of idiocy; hallucinations of sight and sound, with or without mania, precede general cerebral indifference, apathy, and paralysis; the respiration, without the stertor of opium or alcohol, is easy and slow; the temperature of the body is lowered; as the bromism becomes more profound, the patient lies quiet in bed, unable to move or feel or swallow or speak, with dilated and uncontractile pupils, and scarcely any change of the color of his skin or face."

Action on Nervous System.—The persistence of voluntary movement in the frog after the abolition of reflex actions shows that the influence of the drug is not chiefly exerted upon the cerebral centres of motor impulse, nor upon those cells of the cord which originate movement, but upon either the afferent nerves or those portions of the cord which transmit the impulse from these nerves to the cells presiding immediately over motion. This is confirmed by some experiments of Lewisky, in which it was found that previous separation of the cord from the cerebrum had no influence upon the action of the bromide. Both he and Purser also found that death occurred from small doses before the motor nerve trunks and the muscles had lost their irritability (confirmed by Saisson, *Schmidt's Jahrbücher*, Bd. cxliii. p. 17). This being so, the question arises whether the paralysis be spinal or due to paralysis of the peripheral afferent nerves. There is an apparent conflict in the evidence upon this point. Eulenberg and Guttmann (*loc. cit.*, p. 103) found that when access of the poison was prevented to one or more limbs by tying the arteries, reflex actions were abolished in these parts as rapidly as in others. Similar results have been obtained by Lewisky, by Roberts Bartholow (*Bromides: Their Physiological Effects*, Providence, 1871), by Purser* (*loc. cit.*, p. 326), and by Laborde (*loc. cit.*, p. 434). The latter observer has also found that electrical stimulation of a nerve high up will cause violent spasms in the muscles directly supplied by it, although it may be unable to excite the slightest reflex tremor. On the other hand, Damourette and Pelvette assert a contrary result. Unfortunately, they do not give the details of their experiments. They state, however (p. 247), that if the lumbar plexus of vessels be tied before the poisoning, the fore feet lose their reflex activity before the hinder. There are two possible methods of reconciling their results with those of the other observers. In some way the operation may have interfered with the circulation in the lower part of the cord, and consequently the poison have reached more freely the upper part of it and acted first upon it. Again, if the injection was, as is very probable, thrown into the anterior portion of the body, the poison may have reached the anterior extremities in so concentrated a form as to have acted, as it were, locally upon their nerves and muscles. The same observers in another portion of their memoir show that the solutions of these salts travel by imbibition; and this and their local action seem to me to be the cause of the differences of experimental results. It seems well established that cutaneous anæsthesia in greater or less degree accompanies the loss of reflex activity; for, as Dr. Purser says, a poisoned animal quite able to jump submits to pinching, pricking, burning, etc., without moving. Eulenberg and Guttmann have noticed the same thing in some rabbits. Damourette and Pelvette (*loc. cit.*, p. 247) have noticed a condition in which electrical stimulation of a nerve-trunk produced marked reflex action, although no excitement of the skin supplied by the afferent fibres of the nerve was capable of doing this, showing that the extremities of the sensitive nerves are affected before the trunks. The evidence is, I think, sufficient to prove that bromide of potassium affects all parts of the nervous system of the lower animals, but that the cerebrum, the motor tract of the cord, and the efferent nerves are the last portions to be affected; that the most sensitive to its action is the receptive portion of the cord.—that which receives and transmits reflex impulses,—and next to this, and perhaps almost equally susceptible with it, are the peripheral ends of the afferent nerves.

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* From the wording of his memoir, however, it is doubtful whether Purser performed the experiment himself.

Upon the cerebrum of the higher animals the bromides undoubtedly exert an influence, and the researches of Prof. Albertoni (*Arch. f. Exper. Path. u. Therap.*, xv. 256) have thrown much light upon the usefulness of the drug in epilepsy. That observer found that when administered to dogs the bromide depresses very markedly the power of the motor zone of the cerebral cortex to respond to stimuli, and to cause, on decided irritation, epileptic attacks; it was also discovered that this action of the bromide was much more decided when there had been a prolonged saturation of the system with the drug than after a single large or even toxic dose. The intellectual symptoms of bromism show that in man this action on the cerebral cortex is more marked than in the lower animals, on account, no doubt, of the higher cerebral development. The drug in other respects acts upon man as upon other mammals, lowering the reflex excitability of his spinal cord, paralyzing the ends of his peripheral nerves, and otherwise affecting him in the same order and degree.

According to the researches of Dr. B. Schulze, there is under the influence of the bromide a decided decrease in the elimination of phosphorus, an indication that the protoplasmic molecular changes in the nervous system are lessened by the drug (*Zeitschrift f. Biologie*, xix. 301, 1883).

Circulation.—It is well established that large toxic doses of the bromide exert a direct paralyzing action on the heart, lessening both the force and frequency of the beat, and finally causing diastolic arrest.* Dr. J. G. Schouten (*Archiv der Heilk.*, xii. 2, p. 97, 1871; *Schmidt's Jahrbücher*, Bd. cliv. p. 11) found that during the slow injection of a two per cent. solution into the vena cava of a rabbit the cardiac systole grew slower, the diastolic pauses longer, and finally the heart stood still, exhibiting only fibrillary contractions of its walls. The same observer is, so far as I know, the only one who has made manometrical studies of the action of small doses of the drug. He found that such amounts of the bromide administered hypodermically or by the stomach always produced increased pulse-frequency with lessened arterial pressure. His experiments were, however, not carried far enough to demonstrate either how these two changes are brought about, or the relations of the drug to the vaso-motor nerves. Much has been predicated upon the theory which asserts that bromide of potassium causes vaso-motor spasm. No decisive proofs have, however, yet been offered of the truth of this favorite dogma. The evidence so far brought forward is as follows: Lewisky found that if the toes of two frogs—one poisoned, the other not—were cut off, the unpoisoned frog bled much more freely than the other. This experiment has been confirmed by Dr. Amory: it, however, evidently does not prove the existence of vaso-motor spasm, but only that of a lessened activity of the circulation, which may be of cardiac origin.

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* For experiments upon the isolated heart of the frog by Prof. Sydney Ringer, see *Med.-Chir. Trans.*, 1882.

According to Damourette and Pelvette (*loc. cit.*, p. 249), when the interdigital membrane of the frog is watched during poisoning, there is seen at first very often an exceedingly brief period of increased circulation, but in a very short time the latter becomes much slower. Dr. Meuriot (*L'Étude de la Belladone*, p. 49) asserts that by the aid of the microscope this slowing of the circulation can readily be seen to be due to a contraction of the capillaries, and especially of the small arteries, whose lumen may even be obliterated. Dr. Saisson (*Schmidt's Jahrbücher*, Bd. cxliii. p. 17) also asserts that he has witnessed a similar phenomenon in the tongue of the frog, and Dr. Hammond and Dr. Amory state that they have seen it in the brain of the dog. On the other hand, Dr. Purser (*loc. cit.*) and Dr. F. B. Nunneley (*London Practitioner*, vol. iii. p. 351) assert that the vessels in the frog's web are not affected by bromide of potassium given hypodermically.

My own studies of the action of various poisons upon the vessels of frog's web have yielded such varying and unsatisfactory results as to make me hesitate in accepting evidence of this nature unless otherwise corroborated. In the absence of manometrical studies, I think the most that can be fairly claimed is that our present knowledge renders it somewhat probable that the salt under consideration is capable of producing vaso-motor spasm. The further deduction that the nervous symptoms induced are secondary to and produced by this spasm is wholly gratuitous, unproven, and improbable. The action of the bromide when applied locally to the bared nerve demonstrates that it acts directly upon nerve-tissue. Further, the absolute anæmia of the bloodless "salt frog" produces no such nervous symptoms as does even a non-toxic dose of the bromide; and the direct experiments of Dr. A. Weil (*Reichert's Archiv für Anatomie*, 1871, p. 271) have shown that in the frog the complete abolition of circulation has no effect upon the spinal marrow or upon reflex actions during the first half-hour. The proof is very strong that the drug acts directly upon the nervous tissues.

Temperature.—In warm-blooded animals, toxic doses of the bromide of potassium lower very decidedly the temperature. Although the point cannot be considered at all settled, it is probable that this lowering of temperature is due to a direct checking of tissue-changes. Dr. J. H. Bill (*American Journ. Med. Sci.*, July, 1868) has found a constant decrease in the amount of carbonic acid eliminated after the ingestion of the salt. In his experiments, the daily excretion of urea was not perceptibly affected; but Dr. Rabuteau found it slightly lessened (*Gaz. Hebdom.*, 1869), as did also Dr Bartholow (*loc. cit.*, p. 11).

Elimination.—When the blood is charged with the bromide, the salt probably escapes with all the secretions. It has been found by Voisin, Amory, Namias, Bill, etc., in the saliva and in the urine, and by Amory in the perspiration (*Bost. Med. Surg. Jour.*, Oct. 1868). In the body of a man who died whilst taking it, M. Namias (*Comptes-Rendus*, tome lxx. p. 882) found it in all the liquids, as well as in the brain, liver, spinal cord, lungs, etc. Elimination takes place to a certain extent through the skin, and to some extent through the intestinal mucous membrane also. P. Guttmann (*Virchow's Archiv*, lxxiv.) has recognized bromine in the contents of the acne pustules of bromism. Dr. Bill (*loc. cit.*, p. 25) always detected the bromide in marked quantities in the fæces of men taking it; and H. Quincke (*Reichert's Archiv für Anatomie*, 1868, xxxv. 158) found that when forty grains of the bromide of sodium were given to dogs with intestinal fistula, two and a half hours afterwards the intestinal juices were free from the bromides, which reappeared in them from three to six hours later. The salt escapes also through the kidneys. The rapidity of elimination seems to vary: thus, Amory recovered one-half of the amount ingested during the first and one-third during the second twenty-four hours, and Mr. Ware (Thesis of Dr. H. P. Bowditch, *loc. cit.*) obtained a little more than half of the amount ingested in the urine of the succeeding thirty-two hours, whilst Bill was not able to get more than one-eighteenth of it during the first day. Dr. Bill has frequently found the bromides in the urine two weeks after the last dose has been exhibited; and Dr. Rabuteau has seen its presence persist under similar circumstances for a month.

It has been claimed (Prof. Binz, *London Practitioner*, 1874) that the bromide of potassium owes its physiological and therapeutic powers solely to its base. This is plainly not the case, as the bromide is not largely decomposed in the system, and the symptoms caused by it are very different from those produced by carbonate of potash; in a later publication (*Arch. Exper. Path. und Therap.*, xiii.) Prof. Binz himself has shown that bromine vapor produces in frogs effects in many respects similar to those caused by the potash salt. At the same time it is almost certain that the potash influences the system, and that the whole result is produced by a conjoint action of both ingredients of the salt. G. Krosz (*Arch. Exper. Path. et Thérap.*, vi. 43), in three experiments upon man, found decided difference in the results following proportionate doses of bromide and chloride of potassium and of bromide of sodium. He attributes the lessening of reflex activity to the bromine.*

THERAPEUTICS.—The bromide of potassium is employed by the therapeutist to quiet *cerebral excitement* when not inflammatory in its nature; to lessen over-susceptibility of the spinal centres of reflex action, or of the peripheral afferent nerves which lead to these centres; and to subdue nervous excitement of the genital system. The contra-indication to its use is the existence of a high degree of debility or exhaustion.

There are various forms of *nervous excitement* or unrest, such as sometimes follow excessive intellectual toil, anxiety, and other nervous strain, or occur during convalescence from acute disorder, in which the salt now under consideration is very valuable. The same may be said of some forms of *hysteria*. In some cases of *neuralgia* it undoubtedly affords great relief, but in the majority of cases it fails. It has seemed to me useless in neuralgia dependent upon anæmia or want of power; and my experience agrees with that of Dr. Anstie, that it is especially useful in persons of good nervous power, muscular force, and activity of circulation. As a hypnotic, it is employed in wakefulness from nervous excitement and in *delirium tremens*.

The chief use of the bromides is, however, to lessen reflex activity. It is especially in *epilepsy* that it has attained a most deserved reputation, doing far more good than all other remedies combined, sometimes effecting cures, more commonly ameliorating the symptoms, but occasionally failing entirely. There is no known method of distinguishing before trial with any certainty in what cases it will do good. Trousseau (*Clinical Medicine*, Sydenham Society, London) and Bartholow (*loc. cit.*) both assert, however, that it is least efficient in the mild form of the disorder known as the *petit mal*. The most brilliant results have, as a rule, been obtained in cases of not too long duration in which the fits are frequent and severe. The governing principle in its use is to try it in every case, increasing the dose until a mild degree of bromism is induced, and being guided by the results.

The salt is also often efficacious in other reflex spasmodic neuroses; in the *vomiting* of *pregnancy* or of uterine disease; in the *convulsions* of children; and, according to Dr. J. T. Rothrock, in preventing the so-called *urethral fever* induced in very susceptible males by the introduction of the catheter or bougie. The physiological action of the salt seemingly indicates that it is of all known remedies the one best suited for the treatment of *tetanus*. Clinical experience certainly accords with this conclusion; in the table below are collected thirty-four cases of tetanus, nearly all traumatic, in which there were but four deaths. Not less than a half-ounce of the salt should be exhibited in the day, and at night chloral should be used as a hypnotic (see Chloral).

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* Consult also Steinauer's paper in *Virchow's Archiv*, Bd. lix.

The following table contains all the statistical information I have on the subject. Cases not otherwise marked recovered:

REPORTERS.	No.	KIND.	PLACE REPORTED.	REMARKS.
Dr. Bachenal.	1	Traumatic.	London Lancet, Feb. 1869.	
Dr. Derby.	1	"	Boston Med. and Surgical Journal.	Morphia also used.
A. Fergusson.	1	"	Edinburgh Med. Journal, July, 1872.	Chloral also used.
	1	"	U. S. Army Med. Department Circular No. 3, Aug. 1871.	
Dr. Panas.	1	"	Gazette Hebdomadaire, No. 26, 1872.	Opium also used.
Dr. C. L. Bard.	1	"	New Remedies, Jan. 1873.	
Dr. Bruchon.	1	"	Bulletin Thérapeutique, vol. lxxvii. p. 8.	Small bleeding and etherization also used.
Robert Brown.	1	"	Edinburgh Med. and Surg. Journal, vol. xiv., 1869, p. 992.	
Prof. May Figueira.	1	"	Bulletin Thérapeutique, vol. lxxvii. p. 428.	
Ibid.	1	Idiopathic.	Ibid.	
Dr. Panthel.	1	Traumatic.	Deutsches Klinik, p. 21, 1874.	Chloral also used.
Dr. Trenholme.	1	"	Canada Med. Record, April, 1875.	Chloral also used.
Allen Coutts.	1	Idiopathic.	London Practitioner, April, 1871.	Calabar bean also used.
H. F. Andrews.	1	?	* ?	
H. K. Steel.	1	?	* ?	Died.
G. Derby.	1	?	* ?	Took nearly 12 oz of the salt.
Dr. Bakewell.	1	?	* ?	
Dr. Hancock.	1	?	* ?	Died.† 30 grains of the bromide every four hours, with 20 minims of the tincture of belladonna.
R. Southey.	1	Idiopathic.	Trans. Lond. Clin. Soc., x. 146.	Died. Bromide not used freely enough to test its value.
A. Cartaz.	1	Traumatic.	Le Progrès Méd., 1875, 370.	
Levis.	1	Traumatic.	Phila. Med. Times, v. 167.	Chloral also used.
H. Van Buren.	1	Traumatic.	Chicago Med. Journ., Feb. 1880.	Chloral, Calabar bean, and opium also used.
I. W. Lankard.	2	Traumatic.	Virginia Med. Monthly, 1880, 698.	Chloral and opium also used.
Dr. Salter.	1	Traumatic.	London Practitioner, Feb. 1882.	Chloral also used.
Dr. Bourgeons.	1	Traumatic.	Paris Thesis, 1880, No. 260 (Laudouard.)	
Dr. Guichard.	1	Traumatic.	" " "	Died.
Dr. Regnault.	1	?	" " "	
Dr. Brenugat.	3	Traumatic.	" " "	
Dr. Regnault.	1	Traumatic.	" " "	
Dr. Dein.	1	Traumatic.	" " "	
Dr. Gaudon.	1	?	" " "	

In *strychnia-poisoning*, Dr. Saisson has demonstrated its value by experiments on animals, and Dr. Chas. B. Gillespie (*American Journal of the Medical Sciences*, Oct. 1870) and Dr. C. L. Bard (*Philadelphia Medical Times*, June, 1871) have each reported recovery under its use, without vomiting, after the ingestion of three grains of the alkaloid.

In nervous excitement connected with the *genital function*, the bromides are often of great value. When there is actual inflammatory disease, as in *gonorrhœa*, the drug frequently fails to effect the desired end. When, however, there is no organic lesion of the organs or of their nerve-centres, the continued dose almost always succeeds to a greater or less extent. I have found the remedy effective in cases of semi-impotence from over-irritability of the organs causing emission too soon during attempted sexual congress. There is abundant evidence as to the value of the remedy in *nymphomania.* As an adjuvant to other physical and moral measures of relief, the salt may be used with satisfaction in men suffering from masturbation. In nervous symptoms occurring at the time of the menopause or complicating uterine disease, and in the peculiar train of morbid phenomena arising from the forced suppression of the sexual function in vigorous individuals of either sex to whom circumstances have denied marriage, the bromides have almost a "unique power."

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* All the cases marked with an asterisk are taken from Dr. Roemer's paper (*St. Louis Medical and Surgical Journal*, 1873). I believe they were all traumatic.

† Since the belladonna probably did as much harm as the bromide did good, this case ought to be excluded.

Dr. Ch. Bernard (*The Clinic*, Sept. 1874; from *Bulletin Gén. de Thérap.*) affirms that the bromide of potassium in doses of from twenty to forty-five grains a day removes with marvellous quickness *malarial enlargements* of the *spleen.*

ADMINISTRATION.—I have known half an ounce of the bromide to be taken at once without inducing any serious symptoms; and in severe acute cases, as in tetanus and strychnia-poisoning, it is perfectly safe to administer two-drachm doses at short intervals, as the case may require. Almost all the indications for the use of the bromide are best met by the so-called continuous dose,—*i.e.*, by the administration of so much in the twenty-four hours until an effect is induced. Thus, in epilepsy, half a drachm may be given four times a day, to be increased to one drachm (half an ounce a day) if necessary; although as little of the remedy as will suffice to prevent the recurrence of the fit must be used: yet any amount necessary to do this should be given, unless bromism be produced before the paroxysms are arrested. The remedy must be exhibited, in a solution freely diluted, after meals. In some cases it causes diarrhœa, which may generally be checked with small doses of opium.

AMMONII BROMIDUM—BROMIDE OF AMMONIUM. U.S.

According to the U. S. Pharmacopœia, this salt should be prepared by the precipitation of the freshly-made solution of the bromide of iron by water of ammonia, the desired salt remaining in solution. It may be obtained in colorless crystals, but generally occurs in a granular powder, which becomes yellowish on exposure. It has a saline, pungent taste, is readily soluble in water, sparingly so in alcohol. When mixed with mucilage of starch, if chlorine-water be added it becomes yellowish brown; a blue tint would indicate the presence of iodine.

PHYSIOLOGICAL ACTION.—The physiological action of the bromide of ammonium has not as yet been fully investigated; but our present knowledge indicates that whilst in many points it resembles that of the corresponding salt of potassium, in others it differs essentially from the latter. According to Dr. N. Bistroff (*Reichert's Archiv für Anatomie*, 1868, p. 723), when two decigrammes are administered to a frog, a period of quietude and lessened irritability is induced, which after fifteen or twenty minutes gives place to violent tetanic convulsion. Later, all excitability is lost, so that even burning calls forth no recognition; the frog lies in whatever position it is placed in, the spasms become more violent, and death ensues. Similar phenomena have been witnessed by both Bistroff and Amory (*The Physiological Action of the Bromide of Potassium and of the Bromide of Ammonium*, Boston, 1872) in the rabbit and guinea-pig, although in one of Dr. Amory's experiments the guinea-pig died without convulsions having been noted. The curious abolition of reflex action and of sensibility consentaneously with the occurrence of violent convulsions was noted frequently, and death seems always to have resulted from asphyxia. In the experience of Dr. Bistroff, moderate non-fatal doses produced only weakness and uncertain movements in the rabbit.

The bromide of ammonium appears to exert very little influence upon the peripheral motor apparatus. Amory has seen the nerves retain their power of conduction after having been placed in a "strong solution;" and, according to Dr. Bistroff, muscles retain their irritability after five minutes' soaking in a ten per cent. solution. According to the latter observer, the heart always continues beating after death from the drug, and the heart removed from the batrachian and laid in a ten per cent. solution did not in any degree lose its normal activity. Even a twenty per cent. solution dropped upon the bared heart produced only a momentary arrest of the ventricular systole. On the other hand, it is proper to state that Dr. Purser asserts that the heart is soon brought still in diastole in poisoning by this salt, and that the nerves and muscles also lose their irritability sooner than after poisoning by bromide of potassium.

The subject certainly needs further investigation; but it seems to me most probable that the bromide of ammonium exerts less influence upon the muscles than the bromide of potassium, but that in other respects their actions are very similar. The experiments of Amory indicate that the ammonium salt affects temperature and acts on the capillaries in the same way as that of potassium, and that it is also eliminated in a similar manner.

The experiments of Dr. Bistroff show that in the cat, at least, the bromide of ammonium has no especial influence, as has been claimed, upon the superior laryngeal nerves.

THERAPEUTICS.—The bromide of ammonium has been employed by practitioners for exactly the same purposes as the corresponding potassium salt, but certainly has not made its way into general use. Dr. Brown-Séquard commends highly the combination of it and its sister-salt in *epilepsy* as being much superior to either of them alone. He gives sixty grains of the potassium with thirty of the ammonium salt, and claims especially immunity from the disagreeable symptoms of bromism. On the other hand, Echeverria

(*On Epilepsy*, p. 316) asserts that the combination is in no wise superior to the bromide of potassium. Prof. Clark, however (*loc. cit.*, p. 106), from an experience in other than epileptic neuroses, is inclined to coincide with Dr. Brown-Séquard. The disease in which the bromide of ammonium has been most used is *pertussis*. Dr. J. M. Da Costa commends it highly in *acute rheumatism* (*Pennsylvania Hospital Reports*, vol. ii.): a drachm to a drachm and a half of it was given, well diluted, in the twenty-four hours.

Several of the bromides have been studied more or less closely by clinicians or physiologists.*

BROMIDE OF SODIUM, U. S., closely resembles in appearance the bromide of potassium, and has been supposed by Voisin to have closely similar physiological and therapeutic properties. On the other hand, M. J. V. Laborde states (Robin's *Journal de l'Anatomie et de la Physiologie*, 1868, p. 560) that in double the toxic dose of the bromide of potassium he has found that it does not produce any characteristic symptoms in the frog, the guinea-pig, or the dog, and leaves the animal perfectly healthy.

By clinicians the drug has been used to a considerable extent. Dr. Meredith Clymer (*New York Medical World*, October, 1871) claims that it will arrest epilepsy without producing the unpleasant cerebral symptoms of bromism. He gives twenty grains three times a day. Prof. Hammond (*New York Medical Journal*, Dec. 1871) asserts that in epilepsy it is in no wise superior to the potassium salt, but claims that its hypnotic power is much greater. M. E. Decaisne, as the result of the trial of the drug in twenty-seven cases (*epilepsy*, *chorea*, *hysteria*), asserts that its action is the same as that of the potassium salt, except that instead of causing diarrhœa it constipates (*Comptes-Rendus*, No. 17, 1870). Notwithstanding this testimony, my own experience is in accord with the physiological teachings, that the bromide of sodium, although not free from therapeutic value, is not at all equal to the bromide of potassium in subduing excitation of the reflex functions.

BROMIDE OF LITHIUM, U. S., was, I believe, first employed in medicine by Dr. Gibb (*Report of the British Association for the Advancement of Science*, 1864), who recommended it as gently tonic and sometimes diuretic. He used it in very small doses. Attention was first called to its employment in nervous affections by Dr. S. Weir Mitchell, who stated (*American Journal of the Medical Sciences*, Oct. 1870), as the result of his experience, that when administered to the amount of half a drachm to one drachm daily, it acts in some cases of epilepsy after the bromide of potassium has failed, and is generally efficient in about one-half the dose of that salt; also that its hypnotic action is much more decided. Prof. Clark (*loc. cit.*, p. 111) confirms these observations.

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* For *bromides of zinc* and *cadmium*, see *Le Progrès Méd.*, 1877; *hydrobromic ether*, *Robin's Journal*, 1877, *Le Progrès Méd.*, 1877.

Hydrobromic Acid.—A solution of the gaseous compound of bromine and hydrogen in water was first employed as a therapeutic agent by Dr. Wade (*Peninsular Journ. Med.*, Feb. 1875). Dr. E. T. Reichert (*Bost. Med. and Surg. Journ.*, civ. 505) found that its action upon the nervous system and circulation is almost identical with that of the bromide of potassium; but its influence upon the brain cortex was not studied. Moderate doses caused some temporary elevation of the blood-pressure, which Dr. Reichert attributes, without, as I think, sufficient evidence, to vaso-motor spasm of peripheral origin. Large doses were directly paralyzant to the heart and to a less extent to the voluntary muscles. Reflex action is suspended by the acid in the frog, and all portions of the spinal cord and nerves are depressed by the poison; but Dr. Reichert presents experimental facts which indicate that the sensory portions of the cord and the sensory nerves are affected before the motor system by hydrobromic acid as they are by the bromides. A long series of trials which I made with hydrobromic acid in the Epileptic Wards of the Philadelphia Hospital, determined that the officinal acid in equivalent doses acts very much as does the bromide of potassium, but is distinctly more irritant to the stomach, and less apt to produce an eruption of acne or muscular depression. It may be used alone in the treatment of epilepsy, but the combination of it with the bromide has seemed to me the best form of administration; the large dose required, when it is given by itself, in most cases irritates the stomach too much. Under all circumstances it must be well diluted. The officinal *dilute hydrobromic acid* (*Acidum Hydrobromicum Dilutum*, U. S.) represents in each drachm nine grains of the bromide of potassium, and may be given in half- to one-fluidounce doses in a tumblerful of sweetened water.

Bromal Hydrate.—This substance, which has been looked upon until recently merely as a chemical curiosity, is formed by the action of bromine upon alcohol, the alcohol being first converted into aldehyde by losing two atoms of hydrogen, and the bromine then replacing the remaining three atoms of hydrogen. The physiological effects of bromal hydrate have been especially investigated by Drs. John G. McKendrick (*Edinburgh Medical Journal*, July, 1874) and E. Steinauer (*Virchow's Archiv*, Bd. lix. p. 65), Rabuteau (*Gaz. Hebdom.*, xliii. p. 681) and Br. Chrostowski (*Hoffmann und Schwalbe's Jahresbericht*, 1881, 197). After large doses death occurs in a very few minutes, with contraction of the pupil, apnœa, and convusions. After smaller amounts (three grains in a rabbit of three or four pounds' weight) the symptoms are successively, restlessness, dilatation of superficial vessels, contraction of the pupil gradually increasing to a maximum, enormous secretion from the buccal and nasal mucous membranes, greatly increased rapidity of respirations, deepening paralysis, coma, lessened frequency of respirations, anæsthesia, convulsions, and death from failure of respiration. Chrostowski finds that the drug acts directly upon the heart muscle and excito-motor centres, and much more powerfully than does chloral. The peripheral vaso-motor apparatus was apparently not affected by it. What knowledge we have of the physiological action of bromal does not indicate remedial value, and clinical experience with it is still wanting.

CHLORAL—HYDRATE OF CHLORAL. U.S.

Chloral, which is itself not used in medicine, is an oily liquid which at the ordinary temperatures gives off pungent fumes, and which is manufactured by the action of chlorine on alcohol. United with water, this oily liquid is converted into a hydrate.

Chloral Hydrate,* or *chloral* of the U. S. Pharmacopœia, is a volatile, crystalline solid, of a hot, burning taste, insoluble in cold chloroform, but very soluble in water, ether, and alcohol. It occurs generally as transparent, colorless tablets, but sometimes in acicular or even in rhomboid crystals. The compound of chloral and alcohol,—*Chloral Alcoholate*,—which resembles closely the hydrate, can be distinguished at once by its insolubility in water and its solubility in cold chloroform.

If an alkali be added to a solution of chloral hydrate, it breaks up into formic acid and chloroform, which, when water has been the solvent, at once separates in the form of oily drops.

PHYSIOLOGICAL ACTION.—When applied to a part, chloral acts as an irritant; and probably for this reason it sometimes, when given by the mouth, causes vomiting, or even purging. When it is given to man or other mammals in moderate doses, the most prominent result in the great majority of instances is a quiet sleep, as closely allied as possible to natural sleep. The subject can readily be aroused from the lighter degrees of this, waking to full consciousness, but soon dropping off again when left quiet. The pulse is in this degree of action not affected, or is rendered a little slower; the pupil is contracted, but becomes normal so soon as the subject is awakened; the respiration is deep, full, and regular. When larger amounts are given, the sleep is much deeper, and may pass into profound coma; the respirations fall in number; the pulse is weakened and rendered slower, but may become rapid and irregular if the dose has been toxic; the temperature is reduced; the muscular system is relaxed, and both sensibility and reflex action are diminished. If a fatal dose has been given, all these symptoms are intensified: with coma, intense muscular relaxation, weak, thready pulse, and a pupil contracted at first, but afterwards dilated, the animal gradually sinks into death, paralyzed and anæsthetic. The immediate cause of death is generally a paralytic arrest of respiration; but in many cases there appears to be a simultaneous arrest of the cardiac action, and it is very possible that fatal syncope may at times occur. At post-mortem examination, congestion of the meninges and substance of the brain and cord, and of the lungs, is commonly found. The blood is thought by Richardson (*Medical Times and Gazette*, Sept. 4, 1870) to coagulate less firmly than when normal.

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* There is a chloral hydrate containing a very small proportion of water, which is insoluble in the latter menstruum. (*Gmelin's Handbook.*) For a case in which chloral was detected after death in stomach, and for methods of examination, see *Edinb. Med. Journ.*, Oct. 1878.

The most constant and prominent of all the symptoms produced by moderate doses of chloral is sleep: this is without doubt due to a direct action of the drug upon the cerebrum. In most cases, as already stated, it is quiet, but sometimes it is restless, and in man has even occasionally been wildly delirious; although it is somewhat uncertain whether the latter condition may not have been due to impurities in the drug. It seems to be well established that in the milder degrees of this sleep there is no anæsthesia. Demarquay (*Bulletin Thérap.*, tom. lxxvii. p. 307) claims that hyperæsthesia very commonly follows the exhibition of small doses. Bouchut (*New York Med. Gazette*, Dec. 1870), Dieulafoy and Krishaber (*American Journ. Med. Sci.*, Jan. 1870), Giovanni and Ranzoli (*Schmidt's Jahrbücher*, Bd. cli.), and Rajewsky (*Ibid.*) confirm this, whilst Liebreich and Labbée* deny it, and Hammarsten, who has noticed such hyperæsthesia, is inclined to think it apparent rather than real. I myself have seen this hyperæsthesia, and there can be no doubt that it is an occasional, if not a constant, phenomenon. Rajewsky (*loc. cit.*) states that there is in frogs a corresponding period of over-excitability of the reflex centres, and that in rabbits he has noticed a glowing heat borne without much complaint, when pinching would produce violent outcries. In *very large* doses chloral produces anæsthesia; but, unless the amount employed be so great as to be toxic, this anæsthesia is in most cases very trifling.

Motor System.—The paralysis and loss of reflex excitability induced by chloral are not muscular in their origin, for Labbée has found that after death the muscles respond perfectly to galvanism. Both Labbée (*loc. cit.*) and Rajewsky (*loc. cit.*) have found that the motor nerves are in no wise affected by large or even fatal doses of chloral, which must therefore act upon the spinal cord to produce the paralytic phenomena. The experiments of Rajewsky have afforded positive confirmation of the conclusion arrived at by this process of exclusion; for he found that in the latter stages of chloral-poisoning direct irritation of the spinal cord gave rise to much less severe spasms than in the unpoisoned animal. Before this paralytic stage is reached, as already stated, Rajewsky affirms that in the frog there is a period of increased reflex activity, and that at this time stimulation of the spinal ganglia shows that they are more susceptible than normal. According to the observer last named, these phenomena occur just as freely after destruction of Setschenow's centre in the frog as before, and are therefore independent of it.

Circulation.—According to Demarquay, when chloral has been administered to animals there is evident enlargement and engorgement of all their blood-vessels; and Rajewsky* states that he has found sinking of the blood-pressure in rabbits from small as well as large doses of the drug. On the other side, Labbée (*loc. cit.*, p. 341) asserts that the rabbit's ear grows pale after the injection of a very feeble dose. In man, Bouchut has obtained sphygmographic traces, which he thinks indicate a primary increased arterial tension. Nanciao, of Venice, has found the tension normal, but Anstie and Andrews (*American Journal of Insanity*, July, 1871) confirm the results of Bouchut when small doses are employed. Preisendorfer (*Deutsches Archiv*, xxv. 48), in a series of sphygmographic studies, thought there might be a brief primary rise of arterial pressure in man, as in animals, but under the full action of chloral the arterial pressure steadily sinks. After very large doses, according to both Andrews and Da Costa (*Amer. Jour. Med. Sci.*, April, 1870), the tracings indicate decidedly lessened arterial pressure. Whatever may be the effect of small doses (and the point needs further investigation), it seems well made out that, both in man and animals, by large doses the blood-pressure is very much lessened, owing probably in part to vaso-motor paralysis, but in largest measure to an action of the drug on the heart. Various observers state that there is in man and the lower animals at this time slowing of the pulse, which, according to Rajewsky, is, in the frog and rabbit, altogether independent of the inhibitory nerves, occurring equally after as before their section. When toxic doses have been employed, the heart, after numerous pauses, is finally arrested in diastole. Analogy points very strongly to this arrest being due to a direct influence upon the heart-muscle or ganglia, but Labbée affirms that chloral placed freely upon the frog's heart slows, but does not arrest, its beat; and that after section of the cord in the choloralized frog the heart will continue beating for hours. These results obtained by Labbée are, however, contradicted by the more recent and thorough study of the effect of chloral upon the isolated heart of the frog by Dr. Sydney Ringer and H. Sainsbrury, who found that chloral lessened the frequency and power of the spontaneous contractions, and also the excitability of the cardiac muscle, and finally caused a diastolic arrest (*British Med. Journ.*, March, 1883).

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* He has noticed it, however, in a single case, confined to the ears. (*Archives Générales*, 1870, tome xvi. p. 338.)

In poisoning in man, the pulse has towards the last been very feeble, generally rapid and irregular, and even in some cases in which recovery has occurred it has been altogether absent for a time. The experiments of Ringer and Sainsbrury are so concordant with this that I have no doubt that chloral is a *direct depressant to the heart*, and is capable of suddenly and unexpectedly destroying life, precisely as does chloroform.

Respiration.—In full doses, chloral lessens the number of respirations per minute, causing them to become slow and full; and when toxic doses are taken this action becomes more and more marked, until finally the rhythm is very much affected, and the respiration grows very irregular, and sometimes very rapid and shallow, until finally it ceases. As these phenomena occur equally after section of the vagi (Rajewsky), the influence of chloral must be exerted upon the respiratory centre at the base of the brain.

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* The work of Rajewsky was done under Professor Rosenthal, and the results, without the experiments, were published as an inaugural thesis. Of course, half of its value is lost for want of the experimental records, and the subject needs re-investigation. I am acquainted with the pamphlet only through *Schmidt's Jahrbücher*.

Temperature.—A most remarkable action of chloral is upon the temperature; and in this point all observers are in accord with Dr. Richardson, of London, who has seen it fall 6° F. in a rabbit which recovered. Bouchut has noticed a fall of 2° (C. ?) in an infant, and Da Costa and other observers have noticed lesser reductions of temperature in man after therapeutic doses. In a case reported by Dr. Levinstein (*Lancet*, i. 1874), after six drachms of chloral the temperature rose to 39.5° C (102.1° F.), and afterwards fell to 32.9° C. (91.22° F.). Hammarsten has found that the fall of temperature is very rapid, 6° C. in an hour, and that it is dependent upon diminished production of heat, since it occurs equally in animals well wrapped up and laid in a warm place.

The physiological action of chloral may be summed up as follows. Upon the cerebrum it acts as a most powerful and certain hypnotic; in full doses it acts as an intense depressant upon the centres at the base of the brain, and upon the spinal cord, causing slowing and weakness of the heart's action, probably vaso-motor paralysis, slowing of the respiration, and muscular weakness, with a certain amount of anæsthesia; in fatal doses it causes death generally by arresting, through paralysis of the nerve-centres, first respiration, and finally the heart in diastole. Its action in very small doses is uncertain, but there is considerable evidence to indicate that it irritates or stimulates the spinal and the cardiac, and even the vaso-motor, centres. On the vagi and on the motor nerve trunks it has no marked influence.

Action as Chloral.—The conversion of chloral by alkalies in solution into chloroform and formic acid first suggested its use in medicine to Liebreich (*Wiener Medizinische Wochenschrift*, August, 1869); and the theory that its action is really due to chloroform generated by the alkalinity of the blood has been received with favor by Personne and other writers. The evidence by which this theory is to be disproven or established is twofold in its nature, —*i.e.*, chemical and physiological.

Personne (*Journal de Pharmacie et de Chimie*, 1870), by distilling the blood of animals poisoned by chloral at 40° C., a temperature decidedly above that of the body, obtained chloroform; and his results have been confirmed by Pellogio (*Schmidt's Jahrbücher*, Bd. cli. p. 89) and other chemists, so that I think their correctness is not to be questioned. They are, however, not decisive, for it is very possible that the chloroform may be formed during the distillation, owing to the comparatively high heat employed. This evidence is, then, to be thrown out, especially as Hammarsten (*Ibid.*, Bd. cli.) has found that if chloral be mixed with fresh blood and streams of carbonic acid be forced through it, no chloroform can be detected, but if the mixture be heated the latter can be obtained in abundance. Further, in dogs deeply poisoned with chloral the same observer examined the expired air and a portion of the blood without finding chloroform, although when a clyster of the anæsthetic was given to the poisoned animal chloroform could be detected in a few minutes, in both the blood and the breath. In non-chloralized animals to which similar enemata were given, the chloroform could be found in the breath before anæsthesia was induced. Rajewsky (*Ibid.*, Bd. cli.), Amory (*New York Med. Journ.*, 1870), and Von Mering and Musculus (*Berichte Deutsches Chem. Gesell.*, 1875, i. 662) have confirmed these results: so that it may be considered settled that chloral mixed with blood at ordinary temperatures remains unaltered, and that in the most severe poisoning no chloroform can be detected either in the blood or in the expired air. Hammarsten examined the blood and expired air unsuccessfully, for chloral, in dogs poisoned with the drug; but Amory (*loc. cit.*, p. 616) has obtained from the blood acicular crystals, evidently of chloral. The exact fate of chloral in the system can scarcely be considered as established, but it is probable that it is eliminated with the urine, and at least partially in a changed condition. A. Tomascewicz recognized it in the secretion mentioned by means of the delicate isocyanphenol reaction* of Hoffmann (*Pflüger's Archiv*, ix. 35). Feltz and Ritter (*Compt. Rendus*, lxix. 966) believed that they found sugar in the urine of chloralized animals, but both Von Mering and Musculus (*loc. cit.*, 663), and F. Echard† (*Archiv Exper. Pathol. und Therap.*, xii. 276) have shown that the substance which reduces the copper solution will not undergo fermentation, and Von Mering and Musculus have separated it as *urochloralic acid* in colorless, shining needles, often arranged in star-like groups, soluble in water and alcohol, insoluble in ether. The existence of this acid has been confirmed and its chemical properties studied by A. Borntraeger (*Inaug. Dissert.*, Marburg, 1879), and by E. Külz (*Arch. f. Gesammte Physiolog.*, 1882, 506), who found it destitute of hypnotic or other active physiological powers.

The physiological evidence is in strict accord with the chemical in showing that chloral is not converted into chloroform in the system. Whilst chloral produces a longer and more intense sleep than does chloroform, the latter agent acts much more decidedly as an anæsthetic. Again, Djurberg (*Schmidt's Jahrbücher*, Bd. cli. p. 84) has shown that, whilst after chloroform-poisoning biliary coloring-matters appear in the urine, after chloral-poisoning none can be detected, and that when chloral is added to blood outside of the body no destruction of the red disks occurs.

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* Many chemists have failed to find chloral for want of a delicate test. Dr. F. Ogston (*Edinb. Med. Surg. Jour.*, xxiv. 292) affirms that the sulphide of ammonium affords a means of recognizing minute amounts of the drug.

† Echard has also found that chloral will prevent the development of diabetes by the Bernard prick.

As was first shown by Cohnheim, if the abdominal vein of a frog be opened and salt water be injected until almost all the blood is washed out and the circulatory system is filled with the foreign fluid, the batrachian will live from one to three days in apparently perfect health. Both Rajewsky (*loc. cit.*, p. 91) and Lewisson (*Reichert's Archiv für Anatomie und Physiologie*, 1870, p. 346) have found that upon these "salt frogs," with the circulating fluid completely neutral, the chloral acts precisely as in the normal frog.

I think the evidence which has been adduced completely disproves the chloroform theory, and forces assent to the proposition that chloral acts directly upon the organism.

THERAPEUTICS.—The results of the clinical use of chloral are in strict accord with its known physiological action. The indication which it most usefully meets is to *induce sleep*. The more purely nervous the wakefulness is, the more successful is this remedy. When from functional over-excitement of the brain due to excessive mental strain, or from anxiety or other kindred cause, the patient cannot sleep, chloral is by far our most valuable hypnotic. On the other hand, when severe pain causes wakefulness, chloral is of very little value,—at least in doses which I think safe. Sometimes even in these cases sleep will come, but it will very often be a restless, troubled sleep, with moaning or other indications of suffering; and it may be that the patient on awaking will complain that he has suffered more whilst sleeping than when awake.

In the *sleeplessness* occurring at times during *convalescence* from acute disease, chloral is very efficacious. In the early stages of *fevers* it is sometimes of advantage; Dr. Russell (*Glasgow Medical Journal*, Feb. 1860) recommends it especially in the *wild delirium of typhus* in its earlier stages. In advanced fever-cases, when the symptoms are gravely adynamic, I conceive that the use of chloral would be very perilous. In *delirium tremens* it often induces sleep readily, but not rarely it fails, even in large dose. In the sleeplessness of acute puerperal or non-puerperal *mania*, there is abundant testimony to the value of chloral.

Dr. Lyon Playfair (*Lancet*, 1874, vol. i.) has introduced the use of chloral as a means of alleviating the sufferings of parturition, and has been followed to some extent by other practitioners. He affirms that it produces a drowsy state, from which the woman is aroused by the uterine contractions, which are almost robbed of their painful character. So soon as the "pains" begin to be active he administers fifteen grains of the drug, repeating the dose in twenty minutes; thirty grains usually are sufficient, and he has never given more than a drachm during a labor. Towards the close, when the "pains" become very severe, inhalations of chloroform or of ether may be practiced in the usual manner. It is affirmed by other obstetricians that in rigidity of the os chloral is often of great service, by aiding in the desired relaxation, and at the same time materially alleviating suffering.

On the whole, as a pure *hypnotic* chloral is indeed unequalled, and may be used in all cases when no contra-indication exists.

The second indication to meet which chloral may be employed is *to relax spasm.* For this purpose it has been used with advantage in *puerperal* and *uræmic convulsions.* It must be remembered that in many of these cases, although next to chloroform the best palliative, it is only a palliative, and must only be used to quiet the nervous disturbance until other remedies can have time to act. In *tetanus* it has been claimed that chloral is *the* remedy. Dr. Jos. R. Beck (*St. Louis Medical and Surgical Journal,* June, 1872) has collected, of the traumatic form of the disease, thirty-six cases, with twenty-one recoveries, in which chloral constituted the whole or the major part of the treatment. References* are given below to fifty-six cases in addition; so that the figures stand forty-eight recoveries and forty-four deaths. These results do not seem to warrant the high estimate which has been set upon the value of chloral in tetanus. Dr. Macnamara (*Practitioner,* November, 1874) has employed the remedy in a different way from what is usual. Believing that it exerts very little control over the spasms, he has not used it for such purpose, but has used it simply as a hypnotic, giving the patient forty grains of it at bedtime, and only when the temperature rises above 101° F. a single dose of thirty grains in the morning. No other medicine is given, but the patient is made to swallow four ounces of milk with brandy every four hours, one egg being mixed with the milk morning, noon, and evening. He asserts that in this way out of twenty consecutive cases (all traumatic?) occurring in natives of India he has saved seventeen. My own opinion is that no one single remedy affords the best chances in tetanus, but that a combined use of bromide of potassium and chloral should constitute the basis of treatment, the patient also being supported with food to the utmost. In strychnine and other toxæmic convulsions chloral is often of great value.*

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* RECOVERY.—Fergusson (*Edin. Med. Journ.,* July, 1871); Watson (*Lancet,* 1870); Bartlett; May; Ballantyne; Cushing (*Pacific Med. and Surg. Journ.*); Lovegrove (*Brit. Med. Journ.,* 1872, p. 493); Herndon (*Atlanta Med. and Surg. Journ.,* 1873, p. 69); Macnamara (*Indian Med. Gaz.,* April, 1871); Richelot (*Bulletin Thérap.,* lxxxvi.); Lucian Papillaud (*Gaz. Médicale,* 1875, p. 176); Bourdy (*Bull. Thérap.,* lxxxvi.); Cano (*Lancet,* 1876, i. 564); Cauvy (*Bull. Thérap.,* xciii. 186); Durand (*Centralb. Chirurgie,* 1876, 778); Laurens (*Le Progrès Méd.,* 1876, 180); Pugliése (*Jour. de Thérap.,* 1875, 244): cac 1 case; Cargile (*Lancet,* 1877, ii. 158), 3 cases; Boon (*London Pract.,* xx. 161), 2 cases Roberts (*Amer. Jour. Med. Sci.,* lxxiv. 420), 3 cases; Garnett (*Cincinnati Lancet an Clinic,* 1880, 316), 2 cases.

FATAL.—Porta (*Schmidt's Jahrbücher,* Bd. cli. p. 110), 2 cases; Macnamara (*Indi Med. Gaz.,* April, 1871), 6 cases; Baudon (*Bulletin Thérap.,* lxxxvi.), 3 cases; Bl (*Ibid.*), 3 cases; Petit (*Centralb. Chir.,* 1876, 792), 3 cases; Roberts (*Amer. Journ. Me Sci.,* lxxiv. 420), 3 cases; Cruveilhier (intravenous) (*Bulletin Thérap.,* lxxxvi.); Labb (*Ibid.*); Itard (*Schmidt's Jahrb.,* Bd. cli.); Launelongue (*Bulletin Thérap.,* lxxxvi 1874); Verneul (*Bulletin Thérap.,* lxxxvii., 1874); Boon (*London Practitioner,* xx. 161 Boucquier (*Centralb. Chir.,* 1876, 717); Bresson (*Le Progrès Méd.,* 1876, 180); Puglie (*Journ. de Therap.,* 1875, 244): each 1 case.

In *trismus nascentium* Dr. Widenhofer (*Boston Med. and Surg. Journ.*, 1874) recommends it very highly. He says that in the Children's Hospital he formerly lost all his cases, but that by its use he has saved six out of twelve He gives it to a young babe in one- and two-grain doses by the mouth, or, when the spasms prevent, in double the quantity by the rectum. In *chorea* chloral has been used sometimes with great advantage, more often, I think, with the result of simply diminishing temporarily the choreic movements, and sometimes without any effect. In my own experience the movements have generally returned with unabated violence so soon as its exhibition was suspended. As a nocturnal quietant and hypnotic, it would appear to offer very great advantages in cases of *acute chorea* in which speedy death is threatened from the incessant and violent movements; also in cases complicated with fractures, where a temporary lull is of importance.

In *puerperal convulsions* its use in large doses has met with a great deal of favor (see *Phila. Med. Times*, vol. iv.). A half-drachm may be exhibited at once, and half the quantity every hour or two *pro re nata*.

In the *convulsions* of children it has been employed with apparent good; in *cramps* in pregnant women it has been commended by Dr. Morgenstern (*Wiener Med. Presse*, Nov. 1871); in *singultus*, by Dr. Leavitt (*Amer. Journ. Med. Sci.*, April, 1871); in the spasmodic *nocturnal enuresis* of children, also, it may often be used with advantage (Dr. J. B. Bradbury, *Brit. Med. Journ.*, April, 1871); in *laryngismus stridulus* (Dr. Rehn, *Jahrbuch für Kinderkrankheiten*, 1871) and other spasmodic affections; in *spermatorrhœa* at bedtime it is of service (Gascoyne, *Brit. Med. Journ.*, 1872). In *whooping-cough* it would really seem to be of very great value, as has been attested by Drs. Adams (*Lancet*, i., 1870), Murchison (*Ibid.*, ii., 1870), Rigden (*Practitioner*, xxvii., 1870), Waterhouse (*Ibid.*, Dec. 1870), and various French observers. Small doses (two to eight grains), repeated at regular intervals during the day, are often very efficacious. Another plan, especially useful when the paroxysms are very severe at night, is to give a full dose at bedtime. When there is a tendency to bronchitis and pneumonia, chloral must be used with care in these cases, as in large doses it favors congestion of the lungs: yet Murchison saw a very threatening case, complicated with bronchitis and pneumonia, greatly benefited by its exhibition. In *asthma* it has sometimes been of use, but more often it has failed. In *cholera*, Dr. Hall (*Lancet*, May 2, 1874), believing that in the cold stage of the disease there is a condition of intense nervous irritation, has tried the hypodermic injection of chloral with asserted very good results.

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* For a paper discussing relations of chloral to various mostly unimportant alkaloids, see *Arch. Exper. Path. und Therap.*, ix. 440.

The third indication for which chloral has been used is to *relieve pain.* That it will do so when given in very large doses there can be no doubt; but, unless the dose be so large as to be dangerous, my experience of chloral is that it is of little value as an anæsthetic. Its powers in this direction are incomparably less than those of opium, and its habitual use is probably attended with very grave dangers.

Theoretically, chloral might be of use to *reduce temperature.* Its other active properties will probably completely interfere with its use for this purpose in the vast majority of such cases, especially as, in order to check the development of animal heat, the dose must be very large. When, however, there is a high sthenic state of the system, it might be tried with caution; but clinical experience is almost entirely wanting. I know of but a single case (*Med. Times and Gaz.*, Nov. 1869) reported: in this its use is said to have given satisfaction.

Locally a solution of chloral (25 per cent. saturation) has been used with asserted good effects as a stimulant and antiseptic in foul ulcers, buboes, bedsores, etc., especially when the discharge is free. It is also stated that it gives great relief from pain in *uterine* and other *cancers.* Applied to the skin, chloral acts as a powerful irritant, and has been proposed as a vesicant, but is said to cause excessive pain. See *N. Y. Med. Journ.*, xxxvii. 445.

Prof. Oré, of Bordeaux, has proposed *intravenous injections* of chloral as a substitute for ether and chloroform in surgery, and as a means of combating tetanus. His suggestion has been carried out by himself and others in a number of cases with asserted good results. But in other instances it has apparently caused death, and is, in my opinion, absolutely unjustifiable. The risks are twofold. Under any circumstances chloral occasionally acts with unexpected violence, and has caused death even when exhibited by the mouth in what are usually considered safe doses. It is plain that this danger is vastly increased by throwing the whole dose at once upon the heart and nervous system. Every one who has practiced intravenous injections in animals must be aware of the extraordinary results of throwing the poison almost undiluted into the cavities of the heart. Again, chloral exerts a very great influence on fibrin, and has even been used to coagulate the blood in varices; the intravenous use of the drug may, therefore, be productive of thrombi; indeed, M. Tillaux has reported a case in which a venous coagulum was found after death extending up the arm even into the axillary vein, and accompanied by a white heart-clot.*

The *antiseptic* powers of chloral were apparently first noticed by MM. Dujardin Beaumetz and Hirne in 1872 (see *Bulletin Thérap.*, lxxxvi. 224).

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* Any one desirous of following this subject further will find the following references of value:

Archives Gén., ii., 1874; *Bulletin de l'Acad.*, xxxviii., 1874; *Gaz. Méd.*, xlv., 1874; *Gaz. Méd. de Bordeaux*, xiii., 1874; *Gaz. des Hôpitaux*, 1874; *Le Progrès Méd.*, 1874; *Journal de Thérap.*, 1874; *Presse Méd. Belge*, Oct. 1874.

Recently the subject has been investigated by various observers, especially by Dr. Keen and M. Personne (*Phila. Med. Times*, vol. iv.). It has certainly been shown that a solution of twenty to forty grains to the ounce will preserve animal tissues for a great while, and probably indefinitely. Moreover, the finest microscopical structure appears not to be altered by a solution of this strength. Dr. Keen's first experiences led him to hope that as chloral does not materially affect the color of the tissues, it might be useful in the dissecting-room, and subsequent trials of it have confirmed Dr. Keen's first hopes (*Amer. Journ. Med. Sciences*, July, 1875). Dr. Keen has also had great satisfaction in the use of chloral to keep free from odor the urinals of paraplegics and other patients suffering from incontinence.

TOXICOLOGY.—That chloral is a dangerous agent, capable of destroying life, is attested by a number of published cases; but this is true of other drugs; and the practical point to be determined is, Does it ever act out of proportion to the amount ingested? or, in other words, does the ordinary therapeutic dose ever become toxic, and does it ever act in a cumulative, unexpected manner? Abroad, it has very commonly been prescribed in half-drachm and even drachm doses, and in the vast majority of cases without any bad results. That thirty grains is not a safe dose is shown, however, by the case of Dr. Reynolds (*Practitioner*, March, 1870), in which forty-five grains caused most alarming symptoms; by that of Dr. Watson (*Med. and Surg. Reporter*, Jan. 27, 1871), in which eighty grains, given in ten-grain doses spread over thirty-six hours, nearly proved fatal; and especially by a number of cases recorded by Dr. H. W. Fuller (*Lancet*, March, 1871), in some of which very alarming symptoms followed the exhibition of thirty grains, and in one death in a healthy young woman of thirty. Dr. Schwaighofer, of Vienna, records (*Irish Hosp. Gaz.*, 1873) coma and death in a drunkard following the ingestion of half a drachm. Dr. W. H. Lathrop (*Year-Book of Therapeutics and Pharmacy*, 1872, p. 254) records the case of a man previously healthy, but suffering from delirium tremens, who took sixty grains between 12 and 1 P.M., at 2.30 P.M. twenty grains more, and at 3 P.M., no effect being manifest, twenty grains more. His physicians then left him sleepless and complaining only of a slight paralysis of the lower extremities; and almost in a moment he was dead. Other cases might be quoted (see *Berlin. Klin. Wochenschrift*, 1876), but the above are sufficient to show that chloral may kill suddenly and unexpectedly.

An observation of Prof. Vulpian (*Comptes-Rendus*, lxxxvi. 1303) throws much light upon these sudden deaths. He found that galvanization of a divided vagus would cause in a chloralized animal not momentary, but permanent, arrest of respiration, if the centric end was selected, or permanent diastole of the heart if the distal part of the nerve was attacked. It is very probable that in a man under the influence of chloroform or of chloral, death may be precipitated by a slight peripheral inhibitory irritation. I think the practical deduction from the known facts is that twenty grains is the highest safe dose of chloral; that this amount should not be repeated oftener than once an hour, and, when sixty grains have been taken, not again for some hours, unless in very urgent cases, as acute tetanus or violent chorea threatening speedy dissolution. On the other hand, recovery has been reported by Dr. Eshleman (*Philadelphia Med. Times*, Oct. 1870) after the ingestion of four hundred and sixty grains. There are no lesions found after death from chloral which can be considered pathognomonic, but a dark, bloated countenance and other evidences of death from asphyxia have been noted in some cases.

The treatment of chloral-poisoning is identical with that of opium-poisoning, consisting in the free use of alcoholic and external stimulants, such as sinapisms, dry heat, frictions, flagellations, etc., to maintain the circulation, and of shaking, walking, application of galvanism, cold douches, etc., to keep up the respiration. Artificial respiration should always be resorted to before natural respiration altogether fails; and Clemens (*Schmidt's Jahrbücher*, Bd. cli. p. 99) has found that animals asphyxiated by chloral may often be at once aroused by the inhalation of oxygen. Hypodermic injections of strychnia have been recommended on theoretical grounds, and a case is reported by Dr. B. W. Stone (*Louisville Med. News*, xv. 179), in which four hundred and twenty-five grains of the chloral were ingested, and recovery occurred after the hypodermic use of one-fifth of a grain of strychnia in divided doses. Atropia seems to me a very rational remedy, and Dr. I. M. Booth reports a case (*London Lancet*, 1884, i. 468) of recovery after about one hundred and ten grains of chloral under the use of tincture of belladonna. Probably it will hereafter be found that it is very important in all forms of threatening narcotism to maintain the animal heat. Dr. Lauder Brunton has shown (*Journ. Anat.*, viii., 1874) that if the bodily temperature be maintained artificially animals survive doses of chloral usually fatal, or recover consciousness more quickly than is normal after smaller doses. The inference is very obvious that in human chloral-poisoning, by the use of dry external heat, hot blankets, and other devices, the warmth of the patient should be maintained.

Considerable attention has been given both in this country and abroad to the subject of *chronic chloral-poisoning;* and, whilst some affections have been erroneously attributed to the drug, there seems to be no doubt that its long-continued use often does produce serious symptoms. The cases are divisible into two or three groups, which are, however, really artificial, as is shown by the occurrence of cases belonging to two or even three of the groups. The first of these includes those patients in whom the respiration is chiefly affected. The dyspnœa may be slight, and may only be felt at times, as after exertion or after meals; but it may be constant and alarming. Cases of this character are reported by Jastrowitz, by Schule, and by Ludwig Kirn (*Allgem. Zeitschrift für Psychiatrie*, xxix., 1872; *Practitioner*). In one instance (Prof. N. R. Smith, *Boston Med. and Surg. Journ.*, 1871) death from bronchial effusion is believed to have been caused by chloral.

Dr. Kirn affirms (*Berlin. Klin. Wochens.*, xx. 721) that in some cases mental disturbance with hallucinations occurs.

In the second group of cases, eruptions of the skin are the chief manifestations of the toxæmia. In the mildest of these there is no distinct rash, only the occasional appearance of transient red blotches on the face or neck. But a very extraordinary tendency exists towards the production of a rash or discoloration at the slightest cause, so that drinking a glass of wine will produce an intense, even livid, erythematous redness of the face. In other instances there is marked erythema (Schule, *Allgem. Zeitschr. für Psychiatrie*, xxviii.), occurring first in spots upon the face, but extending downwards to the trunk, becoming more and more general, and showing a marked tendency to follow the nerve-trunks. This erythema is seemingly due to vaso-motor weakness, and consequently is allied to other more urgent symptoms seen in chloral toxæmia. Sometimes it invades the mucous membranes, which become red, swollen, and œdematous; and if the glands are involved, as in a case reported by Dr. Chapman (*Lancet*, 1871), the result may be serious. A deeper implication of the vaso-motor and cardiac nervous system was probably the cause of the general œdema, profound weakness, and failure of heart-action in the case recorded by Prof. N. R. Smith (*loc. cit.*). Prof. Smith also calls attention to desquamation of the cuticle and ulcerations about the nails as being present in these cases.

In the third group of cases, petechiæ, ecchymoses, ulcerations, and even high fever and other pyæmic symptoms, are asserted to have been produced by the continuous use of chloral. It seems to me, however, very doubtful whether the drug really was the cause of the symptoms which have been recorded by Crichton Brown, by Monkton, and by Kirn.

The habitual use of chloral as a narcotic has been indulged in, it is asserted, to a considerable extent, and Dr. Geo. F. Elliott reports (*Lancet*, 1873, i. 754) a case in which "delirium tremens" followed the withdrawal of the accustomed draughts.

ADMINISTRATION.—Sufficient has been said as to the dose of chloral. It is best given diluted with a weak syrup.

METACHLORAL is prepared by acting on chloral hydrate with sulphuric acid. The hard white substance which forms after a few days is washed with water and dried by means of chloride of calcium; then mixed with gum it is formed into crayons which are coated with paraffine for external use. It is said to be less irritating than chloral (*Lancet*, i., 1874).

CHLORAL CAMPHOR. Equal parts of chloral and camphor rubbed together produce a clear liquid. Dr. Lenox Browne claims that this "when painted over the painful parts and allowed to dry" gives the greatest relief in *neuralgia*, and that in *toothache* it is equally efficacious. It occasions tingling of the skin, but never blisters, and has been commended in *pru-*

ritus. A drachm of it swallowed by mistake produced very severe prostration, feebleness of the pulse, vomiting, fifteen "coffee-ground" stools, and prolonged narcotism, with brief semi-delirious periods, lasting four days (*Am. Journ. Med. Sci.*, lxxix. 90). Dr. D. B. Simmons, who reports the case, has since found the chloral camphor, in doses of ten to twenty drops, to be very powerful as a sedative narcotic in mania, etc.

Butyl-Chloral Hydrate. The substance brought forward as a remedy by Oscar Liebreich under the name of *croton-chloral hydrate* is formed by the action of chlorine gas upon aldehyde. It crystallizes in small glittering tables,* and is soluble with difficulty in water. It is now stated to be really butyl-chloral, and that when brought in contact with an alkali in solution it breaks up into chloride and formiate of sodium, and bichlorallylene. According to Liebreich (*British Med. Journ.*, Dec. 20, 1873, Feb. 1876), a drachm of this substance, dissolved in water, and introduced into the stomach, produces in the course of from fifteen to twenty minutes a deep sleep, accompanied by anæsthesia of the head. Whilst the eyeball has lost its irritability, and the trigeminus nerve shows no reaction whatever on being irritated, the tone of the muscles remains unaltered. The effect upon the pulse and respiration is also stated to be much less than that produced by equivalent doses of chloral hydrate. Mr. Liebreich declares that the symptoms after large doses are deep sleep, trigeminal anæsthesia, and death by arrest of respiration. The circulation, he affirms, is kept up with great tenacity, and, even if cardiac action, as well as respiration, has ceased, artificial respiration is able to restore the action of the heart immediately, and the life of the animal may thus be saved. Immense doses of croton-chloral produced cardiac paralysis. According to the author just quoted, the value of the drug is in its power of lessening sensibility before producing narcosis. These assertions of Liebreich are not borne out by the seemingly much more elaborate researches of J. V. Mering (*Arch. Experim. Pathol. Pharm.*, Feb. 1875). He found that the sensibility of the cornea was not abolished until the respiration was reduced to one-half its normal rate. In dogs, cats, and rabbits, the blood-pressure was reduced temporarily by small doses, permanently by larger ones. Intravenous injections of sufficient quantity and concentration were followed by immediate arrest of the heart. Altogether, the symptoms caused by croton-chloral seemed exactly parallel with those induced by chloral hydrate. H. Windel Schmidt (*Centralb. Chirurgie*, 1877, p. 210) also found narcosis to precede the anæsthesia of the head. E. Külz has found that butyl-chloral is eliminated as *urobutylchloralic acid*, a substance analogous to urochloralic acid (*Arch. f. Gesammte Physiol.*, xxviii. 534).

Croton-chloral has been highly praised by Liebreich for its powers of relieving neuralgias and other painful affections of the trigeminus. He states that it will afford relief even in severe *tic douloureux*, but is, unfortunately, only palliative. His statements have been confirmed by Drs. J. W. Legg (*Lancet*, 1873), Benson Baker (*British Med. Journ.*, Oct. 1873), J. B. Yeo (*Lancet*, Jan. 1874), Sidney Ringer (*British Med. Journ.*, 1874), and F. B. Lee (*Ibid.*). In a single very severe case of centric tic under my own care, ten grains of the drug have given very decided temporary relief, and compelled sleep. It is usually administered in doses of from five to twenty grains, in syrup. The safest plan is to give five grains every half-hour until thirty grains have been taken or relief afforded. Liebreich uses it according to the following formula: butyl-chloral hydrate, 5 to 10 parts; glycerine, 20 parts; distilled water, 130 parts. Dose, half an ounce, followed in five minutes by a second, ten minutes later by a third unless relief is afforded.

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* For a detailed account of physical and chemical characters, see a paper by E. Schering, *Neues Repertor. für Pharm.*, Bd. xxi. Heft 5, 1872, which I have abstracted into *New Remedies*, vol. ii.

AMYL NITRIS—NITRITE OF AMYL. U.S.

The nitrite of amyl was discovered by the French chemist Balard (*Annales de Chimie et de Phys.*, xii.) in 1844, and the attention of physiologists was called to it in 1859 by Guthrie; but it was not until 1865 that Dr. Richardson, of London, introduced it to the notice of the profession. Since that time it has been a good deal used, but has not been made officinal. It is a yellowish, oily, very volatile liquid, of a very penetrating, persistent, fruity odor. It is prepared by the action of nitric acid on amylic alcohol, or, as it is commonly called, fusel oil.

Physiological Action.—Nitrite of amyl can be absorbed by any surface except the skin, but, on account of its volatility, has hitherto been used in man chiefly by inhalation. Owing to the physical property just alluded to, its action is extraordinarily quick and very transient, it being absorbed and eliminated with great rapidity.

The most prominent symptoms induced when it is inhaled by a man in moderate quantities, are a sense of great fulness and distention of the head, amounting at last to severe pain, and accompanied by intense flushing of the face, a deep, labored respiration, and an exceedingly rapid, violent action of the heart. The succession of these phenomena is so rapid that often they seem to be simultaneous; but it is said that the cardiac disturbance is sometimes very distinctly manifest before the other symptoms. It has been noticed by Peck and confirmed by Ladendorf that objects look yellow to a person fully under the influence of the drug. After poisonous doses the symptoms have been great pallor, dilatation of pupils, excessive muscular relaxation, slow, scarcely perceptible pulse, irregular respiration (*Am. Journ. Pharm.*, 1881, 137).

In the lower animals the first stage of the action is like that just described in man. After this the breathing becomes violently hurried and panting, progressive muscular weakness and diminution of reflex activity ensue, and finally death from failure of respiration,—sensation and consciousness being preserved almost to the last.

A very peculiar symptom is that a long time before death the arterial blood becomes of almost the same color as the venous blood. Convulsions are sometimes present; but in my experience more often the animal is exceedingly quiet throughout the poisoning.

Elaborate experimental studies of the action of the nitrite of amyl upon the circulation in animals have been made by Dr. T. Lauder-Brunton (*Journal of Anatomy and Physiology*, vol. v.,—*Berichte der Math.-Phys. Classe d. k. sachs. Gesellschaft Wissensch.*, 1869), by myself (*American Journal of the Medical Sciences*, July, 1871), and by Dr. Amez-Droz (*Archives de Physiologie Normale et Pathologique*, Sept. 1873, p. 467). The results are so uniform and in such accord that they must be accepted as proven facts.

Circulation.—It has been found by all three observers just mentioned that, although the pulse is very much increased in frequency sometimes from the very beginning, the arterial pressure is diminished, and finally is reduced almost to zero, and that the fall of pressure occurs equally after section of the vagi as at other times. As the number of heart-beats in the uninjured animal is increased rather than diminished, whilst the strength of the individual beat is not perceptibly lessened, it is evident that, at least in the early stages of the poisoning, the diminution of arterial tension is not cardiac in origin, but must be due to dilatation of the capillaries. This conclusion is confirmed by an experiment of Brunton, who found that if the descending aorta was tied high up, no perceptible fall of pressure was produced by the inhalation of the amyl salt until very late in the poisoning, when the heart itself was acted upon by the drug; also by the fact noted by Dr. Amez-Droz and by Gaspy (*Virchow's Archiv*, lxxv. 310), that the vessels of the rabbit's ear and of the frog's web can be seen to dilate when the salt is inhaled.* That dilatation of the vessels takes place in man as well as in the lower animals, is shown by the flushing of the face, as well as by the enlargement of the retinal vessels, noted by Dr. Chas. Aldridge (*West Riding Lunatic Reports*, vol. i. p. 187).

An interesting question which here arises is, whether the dilatation is centric, due to an action on the vaso-motor nerve-centres, or peripheric, due to a direct action upon the muscular coat of the arterioles. I believe it must be peripheral, and not centric, in its origin, since both in my own experiments and in those of Brunton it occurred after the arterioles had been separated from the vaso-motor centres by division of the cord. This fact appears to prove that the fall of arterial pressure is due to a direct paralyzing action of the drug upon the coats of the arterioles,—a conclusion confirmed by our knowledge of the local action of the nitrite upon muscular tissue.

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* A noteworthy fact asserted by Amez-Droz is that after a long period of dilatation the vessels contract again, whether the inhalation be continued or not. I think the explanation of this is simply that, owing to the volatility of the nitrite, it soon all escapes from the dossil of lint on which it is placed for inhalation; an explanation strongly confirmed by a statement of Dr. Amez-Droz, that in these cases a new inhalation was followed by dilatation as before. Amez-Droz says only the arterioles dilate, but Gaspy found that both arterioles and veins were affected.

Bernheim, however, asserts that this cannot be so, and that the dilatation must be solely due to an action upon the vaso-motor centres, because he found that galvanization of the cervical sympathetic still caused contractions in the vessels of the ear of a rabbit to which nitrite of amyl had been given. As pointed out by Pick (*Centralblatt Med. Wissens.*, No. 55, 1873), Bernheim's experiment does not warrant his conclusion. It only shows that the muscle fibres in the walls of the vessels are not so completely paralyzed as to be unable to respond to very powerful stimuli. Dr. W. Filehne (*Pflüger's Archiv*, p. 478, Bd. ix.) dissents from the view here taken; but it seems to me that the fall of arterial pressure after paralysis by section of the vaso-motor nerves absolutely proves that the drug acts locally upon the arterial coats. It is, however, very probable from the general sedative effect of the drug upon the motor centres that it acts also upon the vaso-motor centres; and when the local flushings caused by small doses of the poison are borne in mind, this probability is greatly enhanced. Filehne affirms that when to animals, whose lungs were exposed, inhalations of the nitrite were given, the change of color was not nearly so great as in the ears, and that if the sympathetic had been destroyed in the neck in a rabbit, and the nitrite of amyl exhibited, the vessels on the unwounded side actually became larger than those of the opposite ear. The answer to these results is, that opening the chest must derange most profoundly the pneumonic circulation, and that all observations upon the comparative size of vessels are very apt to be mere guesswork when the change is slight. Moreover, in Schuller's experiments (*Berlin. Klin. Wochenschr.*, No. 25, 1874), after destruction of the cervical sympathetic in a rabbit, inhalations of the nitrite produced still further dilatation of vessels of the ear. In conclusion, it seems to me established that nitrite of amyl does act locally on the coats of the arterioles, although it may at the same time influence the vaso-motor centres.

In man the pulse-rate is enormously increased by nitrite of amyl. In animals the amount of the increase varies, but in the higher groups the rule appears to be increase of the pulse-rate, which is especially decided in the dog. Filehne (*Pflüger's Archiv*, Bd. ix. p. 490) has by a single very ingenious experiment seemingly proved that the acceleration is due to a depressing influence upon the inhibitory centres. He divided the par vagum in a rabbit, employed an electric current to the severed nerves of sufficient strength to bring the pulse-rate to normal, and found that the amyl salt was powerless to affect the rapidity of the cardiac action. Certain experiments performed by Mayer and Friedrich (*Arch. Exp. u. Path. Pharm.*, v. 63) confirm that of Filehne. It is known that sudden asphyxia slows the pulse by exciting the inhibitory centre. Mayer and Friedrich found that this action is prevented by the inhalation of the amyl salt. Then, again, they found that when by compression of the arteries the blood was prevented from going to the head, the nitrite did not increase the rapidity of the pulse, and also determined that the reflex inhibitory slowing of the heart by irritation of a sensitive nerve is prevented by nitrite of amyl. Further, in dogs with a powerful cardiac inhibitory apparatus the primary influence of the nitrite is more marked than it is in rabbits, whose pneumogastrics are very feeble. The sudden, thumping action of the heart so prominent in man when the nitrite is inhaled is therefore probably, at least in part, due to depression of the inhibitory apparatus. There is, however, as pointed out by Dr. Reichert (*N. Y. Med. Journ.*, July, 1881), much reason for believing that in small doses the nitrite acts primarily as a stimulant to the heart. Lauder Brunton long ago discovered that if the aorta be compressed so as to eliminate in great part the influence of the vaso-motor system, the nitrite causes rise in the arterial pressure; and it is perfectly possible for an excessive heart-action to be more than neutralized, so far as the arterial pressure is concerned, by a vaso-motor depression, so that the immediate fall of pressure caused in the normal animal by the nitrite is not proof that the heart may not be stimulated. The question could be readily settled experimentally by studying the action of the drug in minute quantities upon the cut-out frog's heart; at present the physiological evidence only justifies the belief that it is probable that nitrite of amyl in small amount primarily stimulates the heart. It is very certain that finally, if the dose be large enough, the heart-muscle is depressed, and it may be paralyzed, by a direct action of the nitrite.

Nervous System.—I have found (*loc. cit.*), as the result of numerous experiments made in the ordinary methods, that the diminution of reflex activity and of voluntary motion which undoubtedly occurs in toxæmia from the agent now under consideration is chiefly spinal in its origin; since after death the nerves and muscles preserve, though in an impaired condition, their functional power. On the motor centres of the cord the nitrite acts as a direct and powerful depressant, at the same time that it exerts a similar but much less pronounced action on the nerves and muscles, decreasing, but not destroying, their functional life. The diminution of reflex activity is never preceded by a stage of functional excitement. In some animals convulsions do occur, especially when the drug is administered by inhalation; but they are in all probability cerebral, not spinal, and due to the asphyxiating influence of the poison. Over the sensory nerves and centres nitrite of amyl has but little power. They are among the last portions of the body to be affected, sensation being intact until near death, so that the drug is in no sense an anæsthetic. Mayer and Friedrich assert that at first nitrite of amyl increases the rapidity and depth of the respiration by stimulating the respiratory centres. Whether this be or be not correct, it is certain that later the respiratory centres are greatly depressed, the breathing becoming both slow and shallow, and death finally occurring from paralytic asphyxia.

Urine.—Elimination.—Dr. F. A. Hoffmann found (*Reichert's Archiv*, 1872, p. 747) that in the rabbit a hypodermic injection of 0.111 to 0.113 gramme of the drug is enough to cause diabetes. If twice this amount of the amyl salt is used, the sugar becomes very abundant in the urine, and continues to be present for from twelve to thirty hours. Consentaneously with the elimination of sugar there is a great increase in the amount of the urine. In a patient under my care, to whom the salt was given very freely, at no time could sugar be detected in the urine: so that glycosuria is probably induced only by toxic doses. The nitrite is probably oxidized in the system, at least in part, as F. Rohrmann (*Zeitsch. f. Physiolog. Chemie*, v. 233) has found that when nitrite of potassium is administered to the lower animals the nitr*ate* appears in the urine.

Local Action.—Nitrite of amyl causes a progressive loss of functional power in every highly-organized tissue with which it comes in contact. Nerve-centres, peripheral nerves, muscles of organic and voluntary life, all succumb to it alike. If the contact be not continued too long, the tissue may recover even after a total suppression of its function,—a proof that the poison exerts no destructive chemical or devitalizing influence upon the tissues, such as that of sulphuric acid or veratria.

Temperature.—Nitrite of amyl, in whatever way exhibited, if given in sufficient amount, reduces most remarkably animal temperature. I have seen a pigeon perfectly conscious, although its temperature had been brought down by this agent some 13° F. This influence is as marked in fever as in the normal condition of the animal, and is independent of the nerve-centres, occurring after section of the cord, and even after death in those cases in which post-mortem rise or continuance of high temperature normally takes place. I have also experimentally determined that it is associated with diminished excretion of carbonic acid. It must therefore be due to a direct arrest or check of tissue-changes or oxidation within, or without, the blood. The mouth temperature in man is certainly sometimes elevated by the inhalation of the nitrite of amyl. but the rise is a very temporary one. W. A. Manassein and N. Sassczki (*St. Petersb. Med. Wochensch.*, 1879, iv. 392) found, in a number of studies upon normal and fevered men, that whilst the peripheral temperature was at first increased the rectal temperature was always reduced, and after a time even the surface of the body grew cooler. The maximum reduction was reached in one to one and a half hours, and in a case of fever amounted to 3° C.

The vapors of the nitrite have a very marked influence over oxidation outside of the body, as is shown by many facts, of which it is only necessary here to cite the extinguishment of glowing phosphorus by a few drops of the amyl salt diffused through the jar. It cannot be doubted that within the economy the same thing occurs. If, however, the arrest of oxidation was complete, instant death from suffocation would result. The true explanation of the symptoms evidently lies in diminution, not destruction, of oxidation.

When an animal inhales the nitrite of amyl, the arterial and venous blood soon become of a nearly uniform hue, which resembles somewhat that of normal venous blood, but is quite distinct from it, having a chocolate tint. Moreover, this chocolate-colored blood does not assume the arterial hue when shaken with the air. Dr. Arthur Gamgee (*Philos. Trans.*, 1868, p. 589) discovered that as the chocolate color is assumed by the blood the two spectrum bands of the oxyhæmoglobin disappear and are replaced by new bands nearly, but not exactly, in the place of those of acid hæmatin. If ammonia be added to the chocolate blood, the color changes back to a blood-red again, and simultaneously the spectrum-lines regain their normal position. If a reducing agent, such as sulphide of ammonium, be added to the chocolate blood, it is able to deoxidize the oxyhæmoglobin, but, before doing so, evidently removes it from union with the nitrite, since the new bands disappear and those of oxyhæmoglobin reappear in the spectrum before the lines of the reduced hæmoglobin manifest themselves. Dr. Gamgee also found that the nitrite of amyl blood had lost its power of absorbing oxygen, or of yielding oxygen to the air-pump; and that carbonic oxide gas added to the blood did not expel oxygen from it. Having thus determined that a new compound is formed in the blood by the nitrite, Dr. Gamgee finally succeeded in obtaining it in a crystalline form. As he always upon analysis found the nitrite in this compound, he considered it to be a nitrite-oxyhæmoglobin. Recent researches have, however, shown that the spectrum of this new compound is identical with that of *Methæmoglobin* of Hoppe-Seyler (*Zeitsch. f. Physiol. Chem.*, Bd. ii., Bd. iii. 54), so that the identity of the two substances is very probable.

These facts do not seem to me to prove that nitrite of amyl entering into the blood-vessels at once paralyzes the hæmoglobin of the blood-corpuscle and checks all oxidation. As already stated, the experiments of Dr. Gamgee showed conclusively that this new compound yields up its oxygen to reducing agents. Further, the doctor found that when the nitrite blood was brought into contact with prepared guaiacum-paper it still ozonized it, though not so actively as normal. It is evident that the blood-corpuscles retain to a greater or less degree their power of yielding up ozone to bodies desiring it, and are capable of exerting at least this portion of their respiratory function: further, when this ozone is given up and the oxyhæmoglobin changed into hæmoglobin, so far as our present knowledge goes, the hæmoglobin must absorb more oxygen before it can reunite with the nitrite. Evidently, then, absorption of oxygen must take place; evidently the blood-corpuscles must perform their respiratory function; but evidently also they are greatly crippled and impaired in the rapidity and ease of its performance. Hæmic respiration is, in other words, greatly interfered with, but not abolished.

The accord of the results of this chemical investigation with those arrived at by a purely physiological study of the drug is very striking and very beautiful, both teaching the same thing,—lessened, but not absolutely arrested oxidation.

Having ascertained the existence of diminished oxidation in poisoning by nitrite of amyl, the temptation is very strong to attribute all the symptoms produced by it to this arrest. I do not, however, think that this *post hoc propter hoc* argument is justifiable, for the following reasons: In the first place, the nitrate of potassium and other nitrates, according to Dr. Gamgee, act in the same manner upon the blood, yet the symptoms caused by them are very different from those caused by nitrite of amyl. In the second place, when arrest of oxidation is caused by deprivation of oxygen (see article on Nitrous Oxide) the symptoms are very different, the brain and consciousness being always affected before the centres of reflex action, whereas under the influence of the nitrite of amyl the contrary occurs. In the third place, other substances, such as toxic doses of alcohol, check oxidation, but do not cause the same symptoms as does the drug under consideration. The obvious inference seems to me to be that nitrite of amyl acts directly upon the nerve-centres, independent of its influence on the blood.

THERAPEUTICS.—The results of the clinical use of nitrite of amyl are in accord with what has been said of its physiological properties. Its administration in *angina pectoris* appears to have been first suggested to Dr. Brunton (*London Clinical Society's Reports*, vol. iii.; *Lancet*, July 27, 1867) by the sphygmographic tracings giving evidence of arterial spasm in a case of that disorder. As the pathology of these cases of heart-pang is not definitely made out, it seems useless to speculate how the nitrite acts in many cases;* but there is now abundant evidence of its value in relieving almost instantly agony which has resisted all other treatment. This appears also true whether valvular disease or merely functional disorder exists. In cases of advanced fatty degeneration or of very great dilatation of the heart, I think its use would be attended with some danger, owing to its effect upon the heart-muscle. Dr. Foster (*Brit. Med. Journ.*, 1874, i. 77) has found the drug of great service in a case of *cardiac disease* in which there was aortic insufficiency with excessive hypertrophy and severe frontal headache.

Its physiological action would indicate that it should be of service in all cases of spasm of the capillaries, of the bronchial tubes, and of the muscular system generally. Accordingly, Dr. Oskar Berger (*Allgem. Medicin. Central-Zeitung*, May, 1871) and others have used it with very good effect in *migraine* with evident capillary contraction. In *asthma* my own experience of several cases coincides with that of various physicians, that it will often instantly arrest the paroxysm,† especially in those instances in which there are no secondary lesions, such as emphysema and dilated heart.

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* For a case of failure, see *Lancet*, August, 1867.

† For remarkable cases, see *British Medical Journal*, Sept. 30, 1873; also *Butler's Compendium*, part xiii., Jan. 1874.

The convulsion of *epilepsy* is, according to the present theory, due to a vaso-motor spasm at the base of the brain, to correct which the amyl salt would seem to be indicated, as it also is by the mere existence of the convulsion. In advanced stages of the paroxysm it must, however, be used with caution, on account of the obscuring of its early effects by the symptoms of the disease. In the *status epilepticus*, when there is an almost indefinite repetition of the fits, the remedy may be of great use in stopping them. When there is a notable interval in ordinary epilepsy between the aura and the convulsion, the latter can usually, if not always, be entirely prevented (Dr. S. Weir Mitchell, *Phila. Med. Times*, vol. v. p. 553): the patient should carry a small vial containing a few drops of the drug, and inhale it at once whenever the aura is felt.

Dr. Mitchell also calls attention to the value of the nitrite as an aid in diagnosing those occasional cases of nervous disorder in which petit-mal is simulated by attacks really due to passing congestion of the nerve-centres. In these cases nitrite of amyl instead of arresting the paroxysm increases its intensity. Dr. Wm. F. Jenks has found the nitrite efficient in arresting puerperal *convulsions*, but dangerous on account of producing uterine relaxation and post-partum hemorrhage, a result to be expected from the known physiological action of the drug (*Phila. Med. Times*, 1872, vol. ii. p. 404). In *tetanus* nitrite of amyl would seem to be indicated as a spinal sedative, and as controlling excessive tissue-changes and consequent rise of temperature. It has been used, so far as I know, in only three cases (*Lancet*, 1871; *Phila. Med. Times*, vol. v.), all of which recovered, two with the amyl salt alone and the other with it and chloral. In nervous *dysmenorrhœa* the remedy was first used successfully by Dr. Fuckel; it has been highly commended by Dr. Mary Putnam-Jacobi (*New York Med. Rec.*, Jan. 1875) and by Dr. P. Peck (*Deuts. Arch. Klin. Med.*, xvii. 143). Two to six drops should be given when the pain comes on, and repeated *pro re nata*. In *cholera* nitrite of amyl has been tried without, that I can perceive, even a good theoretical reason, and has not seemed to be of service (*London Med. Rec.*, vol. i.). Dr. V. Urbantschitsch has employed it with various results in various irregular cases of *vaso-motor* disturbances, in intermittent *coryza*, *migraine*, etc. (*Wiener Med. Presse*, 1877). I have seen it used in a number of cases of *intermittent fever*, with the invariable result of putting an end to the chill and of not affecting the hot stage.

The increased cardiac action produced by inhalation of the nitrite has led to its employment as a cardiac stimulant, and there is now much clinical evidence in favor of its employment in cases of sudden heart-failure. It has even been given with asserted excellent results in "*fatty heart*" (Osgood, *Am. Journ. Med. Sci.*, 1874, xx. 58) and in *syncope* from hemorrhage (Madden, *London Practitioner*, xii., 1874).* In cardiac failure, during anæsthesia, it has been employed in a number of cases. The peculiar rapidity of its action makes it especially valuable in emergencies, and though further experimentation is necessary before we can understand its use in anæsthesia, clinical experience is sufficient to warrant its cautious administration. Further, by direct experiment Dr. Reichert has found (*Philad. Med. Times*, May 21, 1880) that when by the ethylen bichloride the blood-pressure and pulse-wave in the dog have been depressed almost to zero they are immediately markedly increased by the amyl salt.

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* Consult also *Philad. Med. Times*, iv.; *Psychol. and Med. Surg. Journ.*, Feb. 1875 *Lond. Lancet*, May, 1875; *Med. Times and Gaz.*, Dec. 1874; *Brit. Med. Journ.*, 1877.

The physiological action of the remedy would very strongly indicate it as an antidote in *strychnia*-poisoning. No case of its use for this purpose in man has come to my knowledge, but the experiments of Dr. St. Clair Gray on rabbits (*Glasgow Med. Journ.*, 1871, p. 188) yielded very favorable results, although they were not sufficiently elaborate to decide the matter. In two rabbits to each of which ten drops of the nitrite and half a grain of strychnia were given together subcutaneously, no decided symptoms whatever were induced; whilst one-quarter grain of the alkaloid alone frequently caused death in a single convulsion.

ADMINISTRATION.—As already stated, the method of administration usually employed hitherto is inhalation, from one to three or five drops being placed on a handkerchief and held near the mouth or nose, the handkerchief being removed so soon as a sense of fulness of the head is experienced. I have given it by the mouth, dropped upon a lump of sugar and taken instantly in doses of two or three drops. There is not at present sufficient evidence to enable us to decide as to the maximum amount of the drug which it is safe to give. In a case of cholera (*London Med. Record*, Oct. 1873), Dr. D. B. Smith exhibited hypodermically two drachms in the course of an hour and thirty-six minutes without inducing any serious symptoms, and a dose of a dessertspoonful has been recovered from, emetics being given (*Am. Journ. Pharm.*, 1881, 137). Used with care, the nitrite, although a very rapidly-acting and powerful agent, seems to be safe, since I have never seen either in man or in animals any sudden or unexpected action,—any influence out of proportion to the amount given. It must be borne in mind that the symptoms generally increase in intensity for a minute or two after the withdrawal of the drug.*

NITRITE OF POTASSIUM † has been very carefully and intelligently studied by Dr. E. T. Reichert (*Am. J. Med. Sci.*, lxxx. 180). Doses of six to ten grains in man sufficed to raise the pulse to 110 or 120, with flushing of the face and intracranial throbbing; the symptoms usually began in twenty minutes and lasted several hours, and were in no cases disagreeably severe. Eructations of a phosphorus-like taste were nearly always present. Ten to fifteen grains have produced complete muscular relaxation, livid lips, headache, etc., lasting three hours (*London Lancet*, 1883, ii. 766). In a very elaborate series of experiments upon animals, Dr. Reichert found that the action of the nitrites of potassium and of *sodium* upon the blood-, heart-, and nerve-centres are indistinguishable from those of the amyl salt, except in being much less rapid and more permanent. In cases of *angina pectoris* the duration of the influence of these nitrites makes them especially desirable, and they will probably in practice be found superior to the amyl salt. Twenty grains of the commercial nitrite of sodium has been given without serious effect, but of a pure article, either of the sodium or potassium nitrite, the dose is three grains; five grains have often produced serious symptoms (see *London Lancet*, 1883, ii. 945). At present a pure article is commonly kept in good drug stores. The dose may be repeated every two hours cautiously.

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* For a case in which an epileptic convulsion followed a hypodermic injection of one minim of the nitrite, see *Journ. Ment. Sci.*, xxx. 252. It is doubtful whether the convulsion was caused by the nitrite.

† For a paper on the theory of the action of the nitrite of sodium by Prof. Binz, see *Arch. Experim. Path. and Pharm.*, xiii. 138.

NITROGLYCERINE is the most powerful of the nitrites. The symptoms which it causes in man are giddiness, constriction or other abnormal sensations in the head often amounting to severe headache, choking in the throat, sometimes nausea, rapid cardiac action, with lessened arterial pressure. After toxic doses there is great failure of the heart's action. A single drop of a one per cent. alcoholic solution has produced insensibility, and in the case of Mr. Field, who took two drops, loss of consciousness and of the pulse at the wrist were complete (see *Brit. Med. Journ.*, 1880, i. 406). Dr. Lauder Brunton and Tait (*St. Barthol. Hosp. Rep.*, xii. 140) have found that upon blood coloration, arterial pressure, nerve-centres, and muscles the nitroglycerine acts very much as does the nitrite of amyl. This similarity of action between nitroglycerine and the nitrites has been recently confirmed by Dr. Murrell and Dr. Matthew Hay (*Lond. Practitioner*, xxx. 422); also by A. H. Enocque (*Comp.-Rend. Soc. Biolog.*, 1883, v. 669), and is remarkable, as the nitroglycerine may be regarded as nitrate of glyceryl. It has been shown, however, by Hay, that during its alkaline decomposition it yields nascent nitrous acid, and it can scarcely be questioned that this acid is developed in the blood, and acts upon the system.

The effect of nitroglycerine is certainly more prolonged than that of nitrite of amyl. According to Prof. Korczynski, the maximum effect of a dose in man is reached in from three to fifteen minutes, whilst all effects disappear in three-quarters of an hour (*Schmidt's Jahrb.*, cxciii. 132). Within the last few years nitroglycerine has been used quite largely in the London hospitals, with asserted excellent results, in *neuralgia* and in *angina pectoris*. The practice has found imitators on both continents. The reports are almost universally favorable in regard to the action of the drug in the diseases mentioned, and in *asthma*, *uræmia*, and *puerperal eclampsia*, and other affections in which experience has shown that nitrite of amyl is of value. It is kept in the drug-stores in one per cent. alcoholic solution, the dose of which may be set down as a half-drop, increased to two or three drops if necessary. It is said that this solution is not explosive, but that, unless care be exercised in manipulating it, headache and other unpleasant symptoms are apt to be produced. Mr. Martindale has shown that nitroglycerine is soluble in cacao butter, and it has been proposed to administer it in the form of chocolate lozenges.

According to the researches of Dr. Richardson (*Brit. and For. Med.-Chirurg.*, July, 1867) the *nitrite of ethyl* acts very similarly to the nitrite of amyl; and it can scarcely be doubted that all of the nitrites depend for their physiological activity upon the nitrous acid and have similar physiological properties.

Valerianate of Amyl has been introduced to the medical profession by Dr. W. F. Wade (*Brit. Med. Journ.*, i., 1874), who appears to consider its therapeutic properties about the same as those of valerianic acid. He makes a compound spirit by adding one part of the valerianate to nineteen of alcohol, and to each ounce half a minim of acetate of amyl. Of this he gives eight drops in an ounce of water. The preparation is no doubt an active one, but probably possesses other properties than those of valerianic acid.

LOBELIA. U.S.

The leaves and tops of the indigenous herb Lobelia inflata. The dried plant has a slight irritating odor and a taste at first scarcely perceptible, afterwards burning, acrid, and attended with a flow of saliva. The active principle is *Lobelina*, a yellowish liquid alkaloid, discovered by Prof. Procter, of this city. *Lobelic acid*, a fixed and a volatile oil, gum, chlorophyl, etc., are also present in the drug.

Physiological Action.—Lobelia appears to have the same influence upon the lower animals as upon man. At least Prof. Procter found a grain of the alkaloid to produce in a cat violent emesis, with intense prostration. In man, the symptoms induced by it when freely administered are nausea, soon followed by violent vomiting, accompanied with intense prostration, as is shown by feeble pulse, cold sweats, pale skin, and great muscular relaxation. Purging may or may not occur. Numerous cases of fatal poisoning by it have been recorded. The symptoms are those above mentioned, intensified; in some cases vomiting does not occur, and it is especially under these circumstances that fatal effects have been noted. Burning in the fauces and œsophagus, epigastric distress, in addition to the intense prostration, bordering upon collapse and finally merging into complete collapse, with coma, stupor, muscular tremblings, and in some cases convulsions, precede the fatal termination.

Our knowledge of the physiological action of lobelia is very imperfect; what we have is derived from the researches of Dr. I. Ott (*Bost. Med. and Surg. Journ.*, 1875, *Phila. Med. Times*, vi.). He found that in the frog it produced a gradual increasing palsy, ending in death from paralysis of inspiration. After death the motor nerves were found insensitive, although the muscles were still irritable. He did not determine whether the spinal cord also suffers, or whether the paralysis is solely due to the palsy of the motor nerve. In the rabbit, the symptoms produced by the alkaloid were slowing of the respiration, progressive palsy, fall of the bodily temperature, convulsive seizures, and death from asphyxia. The alteration of the blood-pressure consisted in an immediate fall, succeeded in some cases by a very decided rise of pressure, followed in turn by a fall. The rise of pressure appears to me to have been produced not by the direct action of the poison, but by the asphyxia induced by it. In large doses lobelia seems to paralyze the vasomotor centres, at least galvanization of a sensitive nerve in the poisoned animal failed to induce any rise of pressure. Such doses were also shown to have a paralytic action upon the peripheral vagi.

TOXICOLOGY.—The symptoms of lobelia-poisoning have been sufficiently described. The treatment should consist in washing out the stomach with plenteous draughts of a warm solution of tannic acid, in the free exhibition of opium and of alcoholic and ammoniacal stimulants, and in the use of external stimulation by dry heat, frictions, mustard, etc., precisely as in poisoning from veratrum viride.

THERAPEUTICS.—Lobelia has been used as an emetic; but its depressing effects are so severe as to forbid such employment of it. It has also been employed to relax spasm in various affections, as in pertussis, tetanus, epilepsy, chorea, convulsions, but has been superseded by more efficient and less dangerous remedies. It is often useful in spasmodic *asthma* or in acute *bronchitis* with bronchial spasm, and appears to be expectorant as well as antispasmodic. An infusion (℥i to Oj) has been strongly recommended as a local application in the eczema produced by the rhus toxicodendron, or "poison-vine." The powder is very rarely used; the dose as an emetic is twenty to thirty grains. The dose of the *vinegar* (*Acetum Lobeliæ*—1 to 10, U. S.) is twenty to thirty minims; of the *tincture* (*Tinctura Lobeliæ*—1 to 5, U. S.), as an expectorant, ten to twenty minims,—in the paroxysm of asthma, fʒi to fʒii every half-hour until nausea is induced. The dose of the *fluid extract* (*Extractum Lobeliæ Fluidum*, U. S.) is, as an expectorant, one to five minims; as an emetic, fifteen minims.

GELSEMIUM. U.S.

The root of Gelsemium sempervirens, the *yellow* or *Carolina jessamine*, a beautiful climbing plant of the Atlantic Southern United States, distinguished by its large, axillary, very fragrant, clustered blossoms and perennial dark-green leaves. The very light, fibrous, dirty-yellowish root has a bitterish taste, and contains an alkaloid, *Gelsemia*, in combination with *Gelseminic Acid*, both discovered by Prof. Wormley (*Amer. Journ. Pharm.*, 1870).

The influence of gelsemium upon man is very marked. There is, however, a wide range of susceptibility, some individuals being profoundly influenced by a dose which has no perceptible effect upon another person. After the smallest active dose (five to fifteen minims of the fluid extract), the only symptom is languor; with it may be a little lowering of the force and frequency of the pulse. When a somewhat larger amount is ingested to the languor is added dizziness, disturbance of vision, with, in some cases, a pain over the brows. Ringer and Murrell state that the pupil is contracted, but this is probably an inconstant result. After toxic doses of the poison the muscular weakness is extreme, and in several cases (*Bost. Med. and Surg. Journ.*, 1869, iii., p. 185; 1879, ci. 18) the flexors of the arms have been especially affected. The disturbance of vision is now very marked, double vision, or partial, or even complete blindness may exist; the pupil is widely dilated and immovable; the external rectus muscle is weakened, sometimes sufficiently to produce a marked internal squint; the eyelid droops, and is raised with difficulty or falls in paralytic ptosis. If the patient be able to walk at all, the gait is staggering; the jaw drops, articulation fails; the general sensibility is much impaired; the respirations slow and labored; the pulse feeble and thready; the skin bathed in a cold sweat; the bodily temperature greatly lowered. Sometimes drowsiness is felt after moderate doses of the poison, but consciousness may be preserved in the midst of very severe symptoms, although in all the fatal cases I have met with it was lost before death. The drug acts very promptly, symptoms usually commencing in about twenty minutes after its ingestion, and commencing to subside in two or three hours.

Gelsemium produces in the lower animals symptoms similar to those which it causes in man, with the exception that convulsions are very generally developed. They are not always present, but have been observed in the frog, pigeon, cat, rabbit, and dog. The loss of voluntary power precedes the convulsion, and in the careful experiments of Ringer and Murrell (*Lancet*, 1876, i., p. 83) upon frogs, it was found that the cord was rapidly exhausted by repeated irritations, so that convulsions could not at once be induced. Prof. Bartholow states that in the rabbit, cat, and pigeon the convulsive movements are backward, sometimes amounting to complete somersaults. The close study of the action of gelsemium is best made by taking up the various systems in rotation.

Nervous and Muscular System.—The retention.of consciousness until very late in the poisoning, both in man and the lower animals, shows that the drug has very little power over the higher cerebrum, although the drowsiness and the final loss of consciousness prove that it is not entirely devoid of such influence. The two most prominent symptoms caused by the drug are the convulsion and the paralysis. The first question to be determined is whether the convulsion is cerebral, spinal, or peripheral. That it is not cerebral is proven by its occurrence in the pithed frog (Ringer and Murrell, *Lancet*, 1876, i., p. 83), and below the point of section in mammals with divided spinal cord (Taylor, *Richm. and Louisv. Med. Journ.*, 1875, p. 606); that it is not peripheral is proven by its taking place in the posterior extremities when the lower aorta is tied before the poisoning (Ringer and Murrell). The cause of the convulsions at present remains inexplicable. The theory of diminished resistance (see p. 248) can hardly be received, because in the careful experiments of Dr. Ott (*Philad. Med. Times*, vii., p. 289), a condition of exaggerated reflex activity was proved to precede the convulsive state. Ringer and Murrell conceive that there are present in gelsemium two active and antagonistic substances, one a tetanizant, the other a paralyzant; but in their own experiments and in those of Dr. Ott, gelsemia believed to be pure produced convulsions. Nevertheless, it is notable that Ott found the acid so much stronger in convulsive action than the alkaloid, as to suggest the truth of Ringer's and Murrell's supposition.

The paralysis in poisoning by gelsemia is evidently spinal in its origin, as its development is not affected by tying an artery before poisoning so as to protect a limb (Bartholow, *Lond. Pract.*, v., p. 203; Ringer and Murrell, *Lancet*, ii., 1875, p. 908), and as the afferent and motor nerves and muscles preserve their functional activity until death (Ott, Bartholow,* Ringer, and Murrell). It is a matter of some importance in explaining the spinal action of the drug to determine its influence upon the different portions of the cord. Dr. Bartholow says that "it acts also on the sensory portion of the cord, producing at last complete anæsthesia; but this effect in warm-blooded animals and in man is toxic only, and follows the paralysis of the motor functions." This may be correct, but, so far as I know, has not been experimentally proven.

Respiration.—Gelsemium usually kills by a paralysis of respiration. According to the researches of Burdon-Sanderson and of Ringer and Murrell (*London Lancet*, i., 1876, pp. 490, 560), immediately after the ingestion the extent of the respiration, but not its rate, is increased; very shortly, however, both rate and depth enter a condition of progressive palsy ending in death. The respiratory changes are the product of a direct action upon the respiratory centres, being uninfluenced by previous section of the vagi.

Circulation.—The action of moderate doses of gelsemium upon the circulation is not very marked. That in toxic amounts it depresses both the pulse rate and pressure is abundantly shown by the symptoms of poisoning in man, and by Dr. Ott's experiments upon animals (*Philad. Med. Times*, v.,

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* Dr. Bartholow affirms (*London Practitioner*, v., p. 203): "This experiment indicates that gelsemium destroys the excitability of the sensory nerve before the motor;" but his conclusion seems hardly warranted by his premises, and in his treatise in therapeutics he distinctly avows the centric origin of the paralysis.

p. 691). As the pulse rate and pressure were reduced in these experiments after previous section of all the cardiac nerves and of the spinal cord, it is evident that the poison exerts a direct influence upon the heart. How far the vaso-motor centres are influenced by the drug has not been accurately determined.

Eye.—The influence of gelsemium upon the organ of vision is very decided. Ringer and Murrell affirm that decided non-toxic doses of the drug cause contraction of the pupil. However this may be, marked dilatation of the pupil is a very constant symptom in the poisoning. It has also been discovered by Ringer and Murrell, and confirmed by Mr. John Tweedy (*London Lancet*, 1877, i., p. 833), that the local application of gelsemia to the eye produces violent mydriasis, with paralysis of accommodation. This indicates very strongly that the dilatation is produced in poisoning by the drug through an influence exerted upon the peripheral nerve ending in the eye. The palsy of the external rectus and the ptosis indicate that such action is paralytic, so that it is a probable conclusion that peripheral oculo-motor paralysis is the cause of the dilatation of the pupil. The falling of the jaw and the loss of the power of articulation indicate that all the motor nerves of the head are acted upon by the poison.

THERAPEUTICS.—Gelsemium was originally employed as an arterial sedative and febrifuge in the *malarial fevers* of the South, and subsequently in other *sthenic fevers*. It appears in some way to depress the bodily temperature, but certainly possesses no controlling influence over the arterial system at all comparable to that of veratrum viride and aconite. Dr. Bartholow commends it highly, as in *pneumonia* and *pleuritis*; its influence for good in these disorders would seem, however, to be chiefly associated with its power of lessening the rapidity of respiration and increasing the tendency to perspiration. It does not appear probable that any advantage to be derived from it will counterbalance the dangers attending its employment in the large doses required. In *asthma*, *spasmodic laryngitis*, *whooping-cough*, *nervous cough*, in which it is also recommended by Prof. Bartholow, its employment seems more plausible, as in these cases there is a distinct spasmodic element. The testimony to its value is most marked in cases of *trigeminal*, *ovarian*, and other *neuralgias*. How it does good in these disorders is as obscure as is the nature of the neuralgias. The marked effect of the drug upon the facial nerves would appear to indicate its employment in facial neuralgias, and especially in facial spasmodic affections. In acute mania the drug may be employed in full doses as a calmative.

Mr. Tweedy has drawn attention to the local use of gelsemium (*Lancet*, i., 1877, p. 832) by the oculist as a substitute for atropia, claiming that it may be employed with equal surety as a paralyzant of accommodation and dilator of the pupil, and that it possesses the very great advantage of its influence going off in a few hours. To thoroughly paralyze accommodation, however, it must be used freely; as he states, "To insure paralysis of accommodation within three hours, a solution of at least eight grains [Gelsemia] to the ounce must be used every fifteen minutes for the first hour, and every half-hour afterwards." Employed in this way, I should think there would be some danger of general poisoning by absorption.

TOXICOLOGY.—Dr. I. Ott (*Philad. Med. Times*, v., p. 693) has collected six cases of fatal poisoning; a teaspoonful of the fluid extract being the smallest amount that has caused death in the adult. Prof. Wormley believes that his chemical examinations have shown that in one fatal case the fluid extract ingested could not have contained more than the one-sixth of a grain of the alkaloid.

The treatment of gelsemium-poisoning should be conducted on general principles. Dr. Geo. S. Courtright asserts that morphia is antagonistic, and details a case in which recovery occurred after the ingestion of from one to two teaspoonfuls of the tincture, one and one-half grains of morphia having been given hypodermically and one grain by the mouth (*Cincinnati Lancet and Observer*, 1876, p. 963).

ADMINISTRATION.—The dose of the *fluid extract* (*Extractum Gelsemii Fluidum*, U. S.) is five minims every two hours until constitutional effects are produced; of the *tincture* (*Tinctura Gelsemii*—1 to 6.6, U. S.), ten to twenty minims.

TABACUM—TOBACCO. U.S.

Tobacco in its various forms is so familiar an article of every-day life that I shall not enter upon any description of it. It contains an indifferent camphor-like substance, *Nicotianin*, and a very powerful alkaloid, nicotia, upon which all its physiological properties have been supposed to depend. *Nicotia*, when pure, is a colorless, transparent, volatile liquid, of a strong tobacco-like odor and a persistent burning taste. It is freely soluble in water, which it absorbs readily and largely from the air. Its salts are crystallizable with difficulty.

PHYSIOLOGICAL ACTION.—Upon those persons who are not habituated to its use, tobacco acts as a very powerful depressant, producing horrible nausea and vomiting, with giddiness and a feeling of intense wretchedness and weakness. If the amount taken has been large, to these symptoms are added burning pain in the stomach, purging, free urination, extreme giddiness passing into delirium, a rapid, running, and finally imperceptible pulse, cramps in the limbs, absolute loss of muscular strength, a cold, clammy skin, and finally complete collapse, terminating in death.

Nicotia produces, when taken in minute quantities, symptoms sufficiently similar to those just detailed. Thus, Schroff (quoted by Stillé and by Krocker) found that in doses of from one-thirty-second to one-sixteenth of a grain it caused an intense burning in the fauces, œsophagus, and stomach, which diffused itself as a sense of heat all through the body, and was followed by giddiness, nausea, and some vomiting, with a rapid, feeble pulse, diarrhœa, intense muscular weakness, laborious respirations, icy extremities, partial loss of consciousness, and other indications of impending collapse. Reil (*Journal für Pharmacodynamik*, Bd. ii. p. 203) took one-seventh of a grain of the alkaloid, with the production of burning in the throat and stomach, headache, a feeling of heat in the head, increase of pulse-rate sixteen beats, muscular weakness, and a feeling of oppressed respiration. In one or two instances, violent muscular tremblings have come on shortly after the ingestion of the poison, and ended in general clonic convulsions. In large amounts nicotia acts with lightning-like rapidity. Thus, in a case of suicide, in which an unknown amount was taken (*Taylor's Medical Jurisprudence*, vol. i. p. 393), the man dropped instantly to the floor insensible, gave a deep sigh, and was dead in about three minutes.

When a minute drop (gtt. $\frac{1}{20}$) of nicotia is administered to a frog, the first evidences of local irritation are succeeded in a few seconds by tetanic cramps, in which the front legs are laid forcibly along the side of the trunk, and the feet bent over the back. This position is said by Krocker to be characteristic of nicotia- or conia-poisoning, and to be due to the extensor muscles being more powerfully contracted than the flexors. When very minute doses are administered, according to Vulpian, this general tetanus is replaced by muscular tremblings and irregular convulsions. After a short time the motor excitement in either case is succeeded by complete muscular relaxation, which, if the dose has been toxic, soon passes into general paralysis, and finally death by failure of respiration, the heart continuing to beat after breathing has ceased. The symptoms which the poison produces in mammalia are exactly parallel with those which it causes in the batrachian. The evidences of the pain produced by the intense local irritation caused by the poison are soon succeeded, after a small dose, by muscular tremblings and irregular voluntary movements, during which the animal often falls through weakness, and which rapidly give way to violent tetanic and clonic convulsions; to these succeeds an intense calm, in which voluntary movement is largely but not altogether abolished. In the first part of this stage external irritation still produces convulsions, but later it is without influence. The urine and fæces are usually voided, and sometimes vomiting occurs. The pupils, at first narrowly contracted, now (Krocker) dilate slightly, but not to the normal point. The breathing, which at first was rapid and shallow, becomes distant and fuller, the peripheral capillaries are relaxed and full of blood, and finally paralysis deepens into death. After death the venous system is usually found engorged. The physiological action of the alkaloid can best be studied in detail by taking up the various systems separately.

Nervous and Muscular Systems.—Upon the *cerebrum* nicotia probably exerts very little direct influence. The convulsions* are certainly of spinal or peripheral origin, since they occur, according to the experiments of Krocker, in frogs whose cerebrum has been extirpated. That they are not peripheral is proven by the experiments of Vulpian (*Comptes-Rendus de la Soc. de Biol.*, 1859, p. 151), who found that cutting off all the arterial communication between the hind legs of the frog and its trunk did not affect the development of the convulsions, when the animal was poisoned with nicotia. This has been confirmed by Krocker, who also found that if the nerve-trunk of a limb be divided the convulsions cease in that limb. The convulsions are, therefore, spinal, and the first stage of nicotia-poisoning is one of spinal excitement. The question here naturally arises, Is the paralysis of the second stage due to spinal depression? There is not yet sufficient evidence to warrant a positive decision as to how far the cord is involved in the paresis, but Krocker is probably correct in believing that it is at least to some degree affected, since he found that tying the arteries of a limb so as to preclude the poison from reaching the nerves did not prevent the limb from lying limp and powerless during the paralytic stage.

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* P. Uspensky has found (*Reichert's Archiv*, 1868, p. 525) that these convulsions are not influenced by artificial respiration.

The action of the poison upon the peripheral *nerves* has been definitively settled by the experiments of Vulpian, of Rosenthal (*Centralblatt für die Med. Wissen.*, 1863, p. 738), and of Krocker, all of whom have found that the functional activity of the motor or efferent nerves is more or less completely abolished by the poison. By tying the artery low down in one leg of a frog, so as to protect the peripheral endings, applying the galvanic currents some distance above this point, and comparing the results with those obtained by galvanizing unprotected nerves, Krocker determined that the peripheral endings were paralyzed sooner than the nerve-trunks, although the trunks themselves were finally affected. The peripheral nerve-endings appear to be at first excited, as Vulpian and Krocker have found that muscular tremblings are not prevented by the section of the supplying nerve, and that they even occur in the curarized frog. These fibrillary contractions also occurred when the alkaloid was injected into a leg whose connections with the trunk had been cut off by a tight general ligature. According to Vulpian and Rosenthal, the sensory or afferent nerves retain their activity to the last. Upon the voluntary *muscles* all observers are in accord in asserting that nicotia exerts no influence.

Circulation.—When nicotia is added to freshly-drawn *blood*, the latter assumes a peculiar dark hue, and the microscope shows that the red corpuscles rapidly disintegrate. In nicotia-poisoning the blood is, however, not perceptibly affected. The amount of the alkaloid necessary to take life is exceedingly small, and although the death by asphyxia causes the vital fluid to be everywhere dark, yet the microscope reveals only normal corpuscles. Moreover, Krocker has found that the dark blood rapidly assumes an arterial hue when shaken in the air, and that its spectrum is normal.

The action of the drug upon the *heart* is very complicated, and has not yet been well determined. Upon the cardiac muscle itself the poison appears to have but very little influence; after death from it the heart is found pulsating, and Dr. W. T. Benham (*West Riding Lunatic Asylum Reports*, vol. iv., 1874) found that even the pure alkaloid painted over the cut-out heart of a rabbit or injected into its cavities did not arrest its movements: indeed, on the contrary, the heart, which had ceased action, was stimulated to renewed effort by the application of the drug. Traube found (*Allgem. Med. Central-Zeitung*, 1862) that when a minute quantity of nicotia is injected into the jugular vein of a curarized animal, artificial respiration being maintained, the pulse and arterial pressure at once sink to half their original position, but in about twenty seconds rise rapidly, the arterial pressure attaining a maximum of about two and a half times its normal grade, the pulse also exceeding its original rate. This period of increased tension lasts about a minute, after which the arterial pressure commences to fall, as does later the pulse-rate also, and finally both sink much below their normal position. After many minutes the pulse generally increases its frequency, often to beyond its original position. If during the second stage the pneumogastrics be cut, the pulse instantly becomes very rapid. It would appear probable that the first lowering of the pulse is due to an action on the inhibitory nerve, as is believed to be the case by Rosenthal; but it appears to me that other investigations are required before this can be considered established. Traube, indeed, states that if the pneumogastrics are cut during the second stage the pulse becomes at once very rapid; but he also affirms that previous division of the par vagum does not prevent the slowing of the pulse. In the experiments of Tugenhold (reported by Rosenthal) upon frogs, the primary slowing of the heart amounted at first to a diastolic arrest, which was not prevented by previous division of the par vagum, but did not occur when very large doses of woorara were given. Rosenthal argues from this that nicotia stimulates the extreme peripheral inhibitory apparatus of the heart, —the reason that the curare prevents the primary retardation of the pulse being the paralysis of the inhibitory peripheral filaments which it is believed to cause. It is clear, however, that the results obtained by Rosenthal are difficult to reconcile with the effects of section of the par vagum already quoted from Traube. The method in which nicotia primarily lessens the pulse-rate must therefore be considered as still unsettled. The later increase of the pulse-rate appears to be due to paralysis of the peripheral inhibitory apparatus, since Rosenthal found that in this stage of the poisoning the strongest galvanic currents applied to the pneumogastrics failed to influence the cardiac pulsations. The causes of the rise and fall of the arterial pressure have not been determined, but they are probably connected with the at present undetermined *vaso-motor action* of the drug. Traube found that they both occurred after section of the vagi, and that in these circumstances minute successive doses would produce after each a temporary rise of pressure until a large amount of the poison was given, when the pressure steadily fell. Rosenthal believes that the dilated vessels which various observers have noted in the ear of the poisoned rabbit prove that the alkaloid finally paralyzes the vaso-motor system.

Pupil.—When exhibited in a moderate toxic dose, or when applied directly to the eye, nicotia produces a very marked contraction of the pupil. If, as is asserted by Krocker, the alkaloid contracts the pupils of cut-out eyes, it is evident that the action is a local one. Hirschmann (*Reichert's Archiv*, 1863) has found that galvanization of the divided cervical sympathetic fails to cause dilatation of the pupil. Krocker, in later experiments, has confirmed this in regard to large doses of the drug, but has found that myosis occurs long before the sympathetic is unable to dilate the pupil. This fact renders it probable that the alkaloid paralyzes the peripheral endings of the sympathetic; but it is barely possible that it induces a spasm of the fibres supplied by the oculo-motor so powerful that the sympathetic is unable to overcome it. Be this as it may, it is very probable that the sympathetic paralysis, if it exists, is associated with oculo-motor spasm; but at present we have not sufficient evidence to warrant any definite conclusion.

Abdominal Organs.—Nasse found in his experiments (*Beiträge zur Phys. der Darmbewegung*, Leipsic, 1866) that injections of nicotia into the jugular vein produced a tetanic contraction of all the intestines, which was not affected by section of the vagi or by compression of the abdominal aorta; even the splanchnics were unable to exercise their inhibitory influence, either because they were paralyzed or because the spasm was too intense for them.

In what way the poison is eliminated has not, that I am aware of, been determined, but it very probably escapes with the urine, since, according to Claude Bernard (*Substances Toxiques*, p. 410) the rapidity of the secretion of that fluid is increased.

THERAPEUTICS.—Tobacco has been employed in past times in a large number of diseases, but has almost passed out of sight as a therapeutic agent, and there are only two indications which it is capable of meeting. These are as follows:

To relax spasm.—Imperfect as is our knowledge of the physiological action of tobacco, so far as it goes it indicates very clearly the great power of the drug in quieting violent muscular spasms. The frightful nausea and vomiting which it is so apt to induce, and the occasional excessive violence of its action, have led to its being superseded by less disagreeable and more controllable remedies. It is still, however, employed occasionally in *tetanus*, with asserted good results. In *spasmodic asthma*, if the patient be not accustomed to smoking, one or more strong cigars will very often at once end the attack, or perhaps abort one which is threatening. In *strychnia-poisoning*, tobacco has been used in several cases successfully.

To alleviate pain.—Taken internally, tobacco has no powers of relieving pain at all commensurate with the danger attending its use, and it should never be employed for that purpose. It is different with its local use: thus, it is often added with great advantage to ointments in the case of painful *hemorrhoids;* and in *pruritus* a strong wash of tobacco affords one of the surest modes of relief. It must never be forgotten that its external employment has led to the most serious and even fatal poisoning.* For this reason tobacco ought never to be employed, as it formerly was, to kill vermin on the person.

TOXICOLOGY.—A large number of deaths have resulted from the medicinal use of tobacco, Husemann stating (*Handbuch der Toxicologie*, vol. ii. p. 483) that no less than ten fatal cases have been reported from the use of tobacco enemata alone. Dr. Copland has seen a clyster containing half a drachm produce death (*Dict. of Pract. Med.*, art. *Colic*). Even smoking has caused an acute fatal poisoning. Melsens affirms that the smoke of half an ounce of strong tobacco contains sufficient nicotia to prove fatal.† In the only case of criminal nicotia-poisoning on record, an unknown amount of the alkaloid was forced into the mouth of the victim, causing death in from three to five minutes (*Ann. d'Hygiène*, 1861, ii.). The treatment of tobacco-poisoning consists in washing out the stomach, the free administration of ammonia and alcohol, the hypodermic use of moderate amounts of strychnia, and the employment of such external measures as dry heat, rubbings, etc. If these fail, artificial respiration should be maintained. The excessive use of tobacco produces in some persons serious nervous disturbance, such as insomnia, irritability, general feebleness; the most characteristic symptom is a peculiar irregularity of the heart's action, often accompanied by distinct intermissions. Amaurosis is also sometimes present. Jonathan Hutchinson affirms (*Med. Times and Gazette*, i. 1884, 40) that he has seen this amaurosis recovered from by the use of opium and champagne without the abandonment of the habit of smoking.

ADMINISTRATION.—The dose of tobacco in substance is usually stated to be five grains, which may be given in infusion. In strychnia-poisoning and tetanus the remedy should be exhibited at short intervals until constitutional symptoms are induced.

CONIUM. U.S.

The U. S. Pharmacopœia recognizes both the leaves and the fruit of Conium maculatum. The fruit should be full-grown, gathered while yet green, and carefully dried. The plant is umbelliferous, a native of Europe, but naturalized in the United States. The dried leaves have a strong heavy odor, increased by the addition of an alkali, and resembling somewhat that of mice. They are bi- or tripinnate, and very much incised. The fruits are one to two lines long, roundish-ovate, striated, with five crenated ribs on the outer sides of the easily-separable halves; the odor is that of the leaves. The active principle is *Conia*, a yellowish, oily, liquid alkaloid, highly volatile, of a strong odor similar to that of the urine of mice, and of a very acrid taste. It is freely soluble in alcohol and in ether, slightly so in water, with which it forms a hydrate, and it coagulates albumen; when exposed to the air it undergoes decomposition, becoming first brown, afterwards resinous; heat accelerates the change.

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* For a number of cases, see Stillé's *Therapeutics*, vol. ii. p. 374.

† The activity of tobacco-smoke is connected with the presence in it of other substances than nicotia (see *Comptes-Rendus*, xc. 1538). A. P. Fokker found a large proportion of carbonic oxide, and asserts that animals immersed in the smoke die of poisoning by that gas.

Physiological Action.—The chief symptom produced in man by conia when taken in doses just large enough to impress decidedly the system is great muscular weakness or languor, with some disorder of vision, and giddiness. On attempting to walk, the patient suffers from a feeling as though his feet were made of lead, and he staggers or falls from the refusal of his knees to support him. There is an intense desire to lie quiet in the horizontal position, and, as the eyelids are especially affected, the eyes are kept shut. In some subjects these symptoms are preceded or accompanied by burning in the mouth or fauces, nausea, and even vomiting, besides heat of head, often with a sense of weight or pressure, or even severe frontal pain. The disorder of vision is apparently due in great part to a sluggishness and finally to a paralysis of accommodation. The experiments of Poehlmann (quoted by Husemann, *Die Pflanzenstoffe*, p. 269) show that very grave symptoms may be induced and yet the pupil remain natural; but sooner or later, as the drug gains power over the system, it probably always dilates. The pulse is first diminished, afterwards increased in frequency. In decided poisoning by conium, the symptoms are probably simply those already mentioned, intensified. I have met with accounts of but three fatal cases of such character. In one, that of the mistress of Dr. Hermann Jahn, killed in a few minutes by from ten to fifteen drops of the alkaloid (quoted by Husemann, *Die Pflanzenstoffe*, p. 269), violent palpitation of the heart is said to have been a prominent symptom. The chief symptom in the second case (*Edinburgh Med. and Surg. Journ.*, 1845) was universal paralysis, with total failure of voluntary movement and of the voice before consciousness was lost. Convulsive movements were present very late in the case. Sensation appeared not to be lost until death was at hand.

The third case was in the person of a medical electrician, suffering from blepharo-facial spasm, who took, beginning four hours after the last of a previous series of divided doses of a fluid extract amounting to one hundred and eighty drops, at 4.10, 4.40, and 5.15 P.M. fifty minims (one hundred and fifty in all) of "Squibb's fluid extract." The first dose produced dizziness and muscular relaxation; the second, great muscular weakness, inability to stand, and thickening of speech, without relief of the spasm; the third, immediately, some nausea, and tremors about the chest. At 6.10 there were nausea, intense muscular weakness, partial ptosis, diplopia, and great difficulty of speech; the pulse was 60. Shortly after this he became unable to speak or to swallow. He made signs for electricity, and, on being asked whether the chemical or the faradaic current, indicated the latter, and also the place of application of the electrodes, but was unable to hold one of the latter. Shortly after this, on being raised up, he dropped dead. (*The Sanitarian*, June, 1875.)

In mammals conia produces symptoms parallel with those observed in man, and it probably acts similarly upon all vertebrates. In some animals, however, the convulsions are more prominent than in man; in frogs they are rarely if ever present; in birds they are occasionally so; in mammals they are more frequent,—thus, Ihmsen saw them in twelve out of twenty-three experiments; they are chiefly clonic, but tonic spasms do occur in the hind legs. As the legs are usually affected before the arms in man, so in quadrupeds the hind extremities are usually paralyzed first. Sensibility is maintained to the last. The respiration is generally much affected, and the heart continues to beat after its cessation.

The occasional salivation and excessive sweating of conia-poisoning indicate that the alkaloid escapes with all the secretions, but the kidneys are undoubtedly the chief channel of elimination. Zaleski and Dragendorff have found it abundant in the urine during the first twelve hours of the poisoning; Prevost has seen the urine of poisoned animals cause in a frog the characteristic general palsy, and in a doubtful case this physiological test might decide the diagnosis.

Nervous and Muscular Systems.—All observers agree that the chief symptom produced by conia (*i.e.*, the paralysis) is not due to any direct influence upon the *muscles*, which, indeed, preserve perfectly their contractility up to death. In 1856, Kölliker (*Virchow's Archiv*, Bd. x. p. 228) announced that the failure of motion in conia-poisoning is due to a direct action of the alkaloid upon the *efferent* or *motor nerves*. He first experimentally found that in frogs killed by the drug the application of the galvanic current to a nerve fails to induce contractions in the tributary muscles. He then tied the aorta in such a way as to cut off the supply of blood to the hind extremities, and found that after voluntary motion had ceased in the fore legs, and even after galvanic stimulation of the anterior nerves had lost its influence upon the muscles directly supplied by those nerves, irritation of the same anterior nerves produced reflex contractions in the hind legs, showing that the anterior afferent nerves and the spinal cord still retained functional activity after the loss of it in all those efferent nerves reached by the poison. After repeating these experiments a number of times, he drew the conclusion already given.

His experimental results have been confirmed by Funke (*Berichte über die Verhandl. der k. sachs. Gesells. der Wissensch. zu Leipzig*, Bd. xi. p. 23, 1859), by Guttmann (*Berlin. Klin. Wochenschr.*, 1868, quoted by Husemann), and by MM. Pelvette and Martin-Damourette* (*Gazette Méd.*,

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* M. Tiryakan (*Compt.-Rend.*, lxxxvi. 1344) has affirmed that absolutely pure conia does not affect the nerves, but M. Prevost (*Arch. Physiol. Norm. et Path.*, vii., 1880) has shown that chemically *pure* bromohydrate of conia has this action.

1870, quoted in *Archives Gén.*, 6e sér., t. xvi. p. 88). The latter observers extended the series by severing in a frog all the tissues at the upper part of the thigh except the nerve, and found that when a batrachian so prepared was poisoned with conia, after the paralysis was complete in all portions of the body to which the poison had access,—after stimulations of the poisoned nerves were powerless to excite contraction in the tributary muscles,—the leg which had been protected from the action of the conia upon it responded not only to irritations applied to its nerve, but also to stimuli placed upon distant portions of the body. These same observers also noted that when conia and strychnia were given simultaneously to a frog from one of whose sciatic nerves the circulation (*i.e.*, direct access of the poison) was cut off in either of the manners spoken of, they produced by their conjoint action a commingling of paralysis in all other parts of the body with violent tetanic spasms in the protected leg,—a commingling explainable only on the supposition that the conia paralyzed all the motor nerves to which it had access through the circulation. Since B. F. Lautenbach (*Philad. Med. Times*, vol. v.), Verigo, A. W. Hofmann, Prof. Prevost, H. Schultz (*Schmidt's Jahrb.*, Bd. cxlix. p. 16; Bd. cxcv. 119), and Fliess (*Arch. f. Physiolog.*, 1882, p. 111) have confirmed these experiments, it must be considered as an established fact that the chief physiological action of conia is as a *paralyzer of the motor nerves, and primarily of their peripheral filaments.**

It has generally been believed that conia has little or no influence upon the *sensory nerves;* but Lautenbach affirms that by a large number of experiments he has shown that it impairs very greatly the functions of the peripheral afferent nerves. The nature of the experiments is not indicated in his preliminary report, and until published the evidence cannot be weighed. Before the paper of Lautenbach was published, M. Gubler (*Bulletin Thérap.*, Jan. 1875) called attention to the action of conium in benumbing cutaneous sensibility, detailing especially a case where temporary loss of sensation was produced in the hand by rubbing a cancerous tumor with the extract. According to the observations of Prevost the *glandular nerves* are not affected in conia-poisoning.

The exact influence of conia upon the *spinal cord* cannot yet be considered absolutely determined, but it is most probable that the poison has a feeble depressant action. Dr. Verigo (*Schmidt's Jahrb.*, Bd. cxlix. p. 16) asserts that it is a powerful spinal depressant, and MM. Pelvette and Martin-Damourette (*Archives Gén.*, 6e sér., t. vi. p. 89) say that it acts as an excitant. Dr. Lautenbach (*Proc. A. N. S.*, Philad., 1875), in carefully investigating the subject, failed to obtain, under any circumstances, evidences of excitement of the cord; he did succeed in producing loss of reflex activity where the nerve was protected by tying the artery in the limb, but as in all but two of fifty-two experiments the reflexes in the protected limb were not greatly reduced until just before death, it is plain that any action upon the spinal cord is unimportant and dominated by more powerful influences. The experiments of Drs. A. D. Davidson and D. Dyce Brown (*Med. Times and Gaz.*, July, 1870), which have been cited as favoring the absurd theory of Dr. Harley that the corpora striata are especially affected by the drug, depended no doubt upon an artificial anomaly said to be common in the leg of the cat.

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* H. Tiryakan (*Étude expérim. et chir. sur la Coniine*, Paris Thèse, 1878) endeavors to show that this action of conia is due to an impurity, and not to the alkaloid; but this is, *a priori*, exceedingly improbable, and Prof. Prevost (*Arch. de Physiol.*, Nov. 1880, 40), using the same preparation as did Tiryakan, has found that the motor nerves are affected.

According to the experiments of Lautenbach (*loc. cit.*, p. 451) the convulsions of hemlock-poisoning are cerebral, since, in a number of cases, after division of the cord they were confined to those muscles supplied by nerves arising from that portion of the spinal marrow above the section.

The retention of consciousness so late in the course of poisoning by conia proves that the drug has but little influence upon the *cerebral hemispheres.*

Pupil.—The pupil is generally dilated by conia; but both Von Praag (*Journ. für Pharmacodyn.*, Heft i. p. 31) and Verigo assert that the phenomenon is not constant, at least in animals. The ptosis of conia-poisoning indicates that the dilatation of the pupil is due to oculo-motor paralysis. The known action of the drug upon nerve-trunks indicates that this paralysis is peripheral,—a conclusion corroborated by the experiments of Dr. I. Hoppe (*Die Nervenwirkungen der Heilmittel*, Heft i., Leipsic, 1855), who found that when conia was dropped into the eye of an animal it caused at first contraction, apparently due to the intense irritation, and afterwards dilatation, of the pupil.

Temperature.—Verigo, Von Praag, and others affirm that lethal doses of conium cause a decided lowering of temperature; but Lautenbach asserts that the drug decidedly increases the temperature both when in therapeutic and in toxic doses.

Circulation.—No sufficient investigation has as yet been made upon the action of conia upon the circulation. Lautenbach states that the arterial pressure falls immediately after the injection of conia, and afterwards rises far above the normal point, and that the pulse is at first accelerated, but afterwards retarded. The secondary rise of pressure was probably due to asphyxia. The primary pulse acceleration is explained by the observation of M. Pelénard, confirmed by M. Prevost, that the pneumogastrics are paralyzed before the motor nerves. M. Prevost finds that the heart itself is scarcely affected at all by the poison.

When locally applied in a concentrated condition, conia probably is fatal to all the more highly organized tissues. Certainly Christison (*Edinburgh Philosophical Transactions*, vol. xiii.) proved this to be so in regard to the muscles which are not influenced by it when taken internally. Upon the mucous membranes it acts as an intense irritant.

THERAPEUTICS.—The paralytic action of conium naturally suggests its use in spasmodic affections; and accordingly it has been tried in *chorea*, in *paralysis agitans*, in *whooping-cough*, and in other diseases of similar nature. Although it seems not to have met with continued favor, and is but little used, it may be employed when life is threatened by the mere convulsive actions, as it will suspend these for the time being. If Dr. Harley's views as to its physiological action be correct, it ought to be especially useful in all motor disturbance connected with irritation at the base of the brain. Clinical proof is, however, nearly as scarce as physiological in this matter.

In maniacal and hysterical excitement, the drug in full doses is said to produce a condition of calm and relaxation which is highly favorable; and in the treatment of the insane, conium is very much used by some alienists (*Amer. Journ. of Insanity*, April, 1873).

Conium has also been employed to relieve pain. As a deobstruent and alterative it has been very largely used, both locally and internally, in *neuralgia* and *sciatica*, with asserted occasional success, in *cancerous* and other *tumors*, in *chronic glandular enlargements*, *swollen joints*, and in various *chronic ulcerations*. Dr. H. Kennedy (*Dublin Journ. Med. Sci.*, Jan. 1874) especially commends it in *chronic rheumatism*, and as an aid to cod-liver oil, etc., in *chronic phthisis*. It has also been employed to arrest the secretion of milk and to relieve *dysuria*. The various uses of conium as an alterative certainly have no definite physiological basis, but they appear to be justified to some extent by clinical experience.

ADMINISTRATION.—One of the great practical drawbacks to the use of this drug is the uncertainty of its preparations. The dose of the *abstract* (*Abstractum Conii*, U. S.) is one to two grains; of the *extract* (*Extractum Conii Alcoholicum*, U. S.), one grain; of the *tincture* (*Tinctura Conii*—1 to 6.6, U. S.), fʒss to fʒi; of the *fluid extract* (*Extractum Conii Fluidum*), ♏j to ♏ii; all of which must be administered in increasing doses until some effect is experienced. Of these preparations, the last is certainly the best. The English *Succus Conii*, so praised by some writers, I have known to be used by the ounce without effect.

The variability of all the preparations has its origin—first, in the varying amount of the active principle in the drug; secondly, in the great volatility of this principle; and thirdly, in the proneness of the alkaloid to undergo spontaneous decomposition, even when kept under the most favorable circumstances, and to a much greater extent when exposed to light and air. The alkaloid, on the whole, would probably be the best form in which to use the remedy; but it is not officinal; abroad, however, it has been used to a considerable extent. Its unstable nature, however, is an obstacle to its use, and has caused M. Mourrut to propose its hydrobromate, which is said to be a crystalline stable salt (*Bull. Thérap.*, xc. 446, xci. 1). The dose of the alkaloid or its salt is one-twentieth to one-twelfth of a grain, which may be dissolved in alcohol.

Toxicology.—Sufficient has been said about the symptoms caused by conia. After death from it no distinctive lesions are to be found, only the usual indications of death from asphyxia. The treatment consists in the immediate evacuation of the stomach and the exhibition of tannic acid,—the tannate formed is, however, probably more or less poisonous,—with the use of external heat and of internal stimulants; artificial respiration should be steadily maintained so long as there is the faintest indication of cardiac action. No physiological antidote is known; but it is possible that atropia might be of service by aiding to maintain the respiration.

CLASS XI.—ALTERATIVES.

THERE are employed by practitioners of medicine, to affect certain diseases most intimately connected with the processes of nutrition, various substances which do not, at least in the doses commonly used, produce any very obvious symptoms. These drugs may perhaps neither stimulate nor depress, so far as can be perceived, any function of the body; their action may be silent and imperceptible, their mode of influence may be unknown; but their therapeutic effects are among the most assured of clinical facts. It is to medicines of this character that the name of *Alteratives* has been applied, because when administered they seem simply to alter morbid processes.

Speculation has been rife as to the mode in which alteratives influence the body; and as the accepted pathology has been humoralistic or otherwise, so has it been strenuously argued that they act upon the vital fluid or upon the solids of the body. The term "purifying of the blood" has been especially applied to their action, and is sufficiently suggestive of their function as viewed from the pathological stand-point of the old humoralist. What we know of the action of these medicines at present amounts to this, that they modify the nutritive processes of the body. As the *physiologist* has scarcely learned the alphabet of that part of his science which treats of the general nutrition, having no knowledge as to what is the real dominant force in the nutritive processes,—as he is unable to tell with certainty in what organs the universal vital pabulum, the blood, is formed, much less to point out the method of its formation and the laws which govern its development,—as the *pathologist* is completely baffled in attempting to find the essence, as it were, of the morbid processes which are successfully met by alteratives,—as he cannot point out to us what perverted functions underlie these diseases as their basis,—why should the *therapeutist* be expected to explain the rationale of his treatment? The empirical facts of the clinical pathologist are met by the empirical facts of the clinical therapeutist. It is absurd to gaze into mid-air for the crowning spire before the foundation-stones of the temple are laid.

To deny, as has been done, the existence or value of medicines of this class because we cannot tell why mercury relieves syphilis or why iodide of potassium cures rheumatism, is as absurd as to deny the existence of the syphilitic and the rheumatic dyscrasia because we do not know their ultimate nature. Let us be content, until more light comes, to hold fast to the clinical facts, each believing for himself, if he choose, that alteratives alter nutrition by affecting the functions of the blood-making organs, or, if he prefer, that they act by impressing the cells of the body directly; or, what is even more philosophical, each holding his mind free from belief, an unoccupied tablet on which the truth may readily be inscribed when it is discovered.

ACIDUM ARSENIOSUM—ARSENIOUS ACID. U.S.

White Arsenic, or *Arsenic*, as first prepared by sublimation from the ores, is in transparent masses, but on keeping becomes milk-white externally. It is soluble in water, has a vitreous fracture, is odorless, of a faint sweetish taste, and volatilizes without fusion "at a temperature not exceeding 400° F." When it is put upon red-hot iron it emits a garlicky odor, owing to its being first reduced to a metallic state and then volatilized.

PHYSIOLOGICAL ACTION.—When applied to any part in a concentrated form, arsenic is a very active escharotic, and even when very much diluted it is a severe irritant. When a single dose of just sufficient size to be felt is ingested, colicky pains, diarrhœa, and perhaps nausea result. After a very large toxic dose, in from one-quarter to three-quarters of an hour an intense burning pain is felt in the œsophagus and stomach, soon spreading to the whole belly, and often accompanied by a sense of constriction at the throat, and an acrid, metallic taste. In a very short time violent vomiting and purging come on. The matters rejected are at first mucous, and variously colored by the contents of the primæ viæ; but they soon become bilious, and often yellowish or greenish, and finally serous, with mucoid flakes and a greater or less amount of blood. As the case progresses, the symptoms mentioned increase in intensity, and to them are soon added others of different nature. The thirst is excessive; the urine is suppressed; the extremities are icy cold; the pulse is small, feeble, and frequent; the rapid and labored respiration is very much embarrassed and painful from the abdominal tenderness; the surface is dark and cyanosed; violent cramps add their torture; exhaustion deepens into collapse; convulsions or coma ensue, and death occurs in from five to twenty hours.

In another set of cases, when the dose has been smaller or the subject less susceptible, the termination is not reached so soon. After symptoms similar to but less violent than those just described have lasted from a few hours to one or two days, a remission occurs; the purging and vomiting grow less frequent, or perhaps intermit; even the abdominal tenderness may in great measure disappear, but the persistent thirst, cold extremities, and suppressed urine show that the danger is not overpast, and after a time the case puts on a more alarming aspect. The belly becomes very tumid, the abdominal pain more severe, difficulty of respiration develops itself, the face is swollen and cyanosed, nervous symptoms, tremblings, cramps, and convulsions appear, and finally an icy coldness pervades the frame, and death occurs in from two to six days. The mind is generally clear to the last. If the patient survive long enough, an eruption very frequently appears, sometimes as early as the second day, sometimes not until the fifth. Its character is various: thus, it may be petechial, urticaria-like, papular, vesicular, or pustular (*Histoire des Éruptions arsénicales*, par Dr. Imbert-Gourbeyre, *Monit. des Hôpit.*, 1857).

Such are the ordinary symptoms of arsenical poisoning; but anomalous cases are not rare. Sometimes profound and rapid collapse, without abdominal pain, has occurred; in other cases heavy sleep, deepening into coma, is said to have been the most marked symptom. Sometimes arsenical poisoning very closely resembles cholera, and it has been mistaken for it not only in life, but also after death, on the post-mortem table (*Virchow's Archiv*, 1870, Bd. l. p. 456).

When arsenical poisoning is not fatal, the convalescence is apt to be slow, and interrupted by various disorders. Prominent among these are affections of the alimentary canal, due to the structural changes produced by the poison. Nervous symptoms are common, and may affect the motor or sensory sphere separately or combined. In some cases they have developed very suddenly (*N. Y. Med. Journ.*, 1850, 177). I have seen anæsthesia of the feet as the only symptom; motor paralysis may exist alone, but it is usually accompanied by anæsthesia, hyperæsthesia, loss of temperature sense, great feeling of coldness, or other disorder of sensation, and not rarely excessive pain, which may be aching or lancinating. Occasionally there are severe cramps. The normal sensibility is usually regained before normal motility. Of one hundred cases of arsenical paralysis collected by Imbert-Gourbeyre (*Des Suites de l'Empoisonnement Arsénicale*, Paris, 1881), in more than half all the extremities were affected; about one-fourth part were paraplegic; in the remainder there was hemiplegia or local palsies. Most frequently the paralysis was not pronounced above the elbow or knee. The lamed muscles are usually sensitive to pressure (C. Gerhard, *Sitzunsb. Physik. Med. Gesellsch. Würzburg*, April, 1882),* and undergo rapid atrophy, losing very early their electro-muscular contractility, or presenting the "reactions of degeneration." This poisoning resembles very closely sub-acute poliomyelitis, but differs in the frequency of pain and other sensory disturbances, and in the tendency towards more or less complete recovery (only three out of one hundred failing, Imbert-Gourbeyre). When sensory disturbance is absent the resemblance is very close. The lesion is probably spinal, and it is scarcely to be doubted that the motor cells of the cord are diseased, for Dr. N. Popow found in dogs killed in a few hours by a dose of arsenic, the spinal cord inflamed; after slower poisoning there were masses of "exudate" in the neighborhood of the blood-vessels, and in very protracted cases the walls of the spinal arterioles were found to be thickened, and the large cells of the gray matter profoundly altered. The protoplasm first became opaque and granular; the nuclei grew fainter and fainter, and finally disappeared; vacuoles appeared, and encroached more and more on the shrunken body of the cell, which finally disappeared (*Virchow's Archiv*, Bd. xciii.).

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* Consult also Renner, *Ueber Ein Fall von Chron. Arsenvergift. Würzburg*, 1876; W. P. McIntosh, *N. Y. Med. Record*, Feb. 1885, 145; Seguin, *Journ. Nerv. and Ment. Diseases*, Oct. 1882, vii. 665; C. K. Mills, *Trans. College of Physicians of Philadelphia*, 3d series, vi.; *Archives de Physiolog. Norm. et Path.*, 1884, iv.

The most obvious lesions found after death from acute poisoning by arsenic are in the stomach and bowels, even when the poison has found entrance through other channels into the system. The gastric mucous membrane is usually swollen, maculated with patches of a deep-crimson or, more commonly, brownish-red color, and is often softened and covered with a diphtheritic exudation, but is rarely ulcerated. Perforation is exceedingly uncommon. The mucous membrane of the upper part of the small intestine, and sometimes of the whole of it, is in a condition similar to that of the stomach. In some cases the lesions very closely resemble those of cholera, as was first pointed out by Prof. Virchow (*Virchow's Archiv*, Bd. xlvii.). In the microscopic examination of a cadaver whose bowels were filled with a "rice-water" fluid, that observer found in the intestinal contents epithelial flakes, and the fungus described by Klobs as peculiar to, and, indeed, the cause of, cholera. The epithelial cells of the mucous membrane were choked with granules, and many of them in an advanced stage of fatty degeneration; the interstitial tissue was full of large round granulated cells; the solitary glands and Peyer's patches were very much swollen. These facts have been confirmed by Dr. Hoffmann (*Virchow's Archiv*, Bd. l. p. 456). The gastro-intestinal lesions produced by arsenic are not due solely or largely to its immediate local effect, since they occur equally when the animal is killed by injection of the poison into a vein. The local influence of the drug is, however, probably not altogether lost, since Unterberger (*loc. cit.*) found that a larger dose was required to kill an animal by venous injection than by exhibition by the mouth.

There is usually in arsenical poisoning a wide-spread granular or fatty degeneration of the tissues. M. Karajau (Tardieu, *Sur l'Empoisonnement*, p. 335) reports a case, which had been mistaken during life for acute atrophy of the liver; Fr. Grohl and Fr. Mosler (*Virchow's Archiv*, Bd. xxxiv. p. 213) one in which they found fatty or granular metamorphosis of the glands and epithelium of the stomach and intestines, of the cardiac muscle, of the diaphragm, of the cortical portions of the kidney, and, to a slight extent, of some of the voluntary muscles; Dr. I. I. Pinkham (*Boston Med. and Surg. Journ.*, 1878, 358) one in which the liver, kidneys, and epithelial lining of the peptic glands were almost destroyed; similar lesions have also been reported by M. V. Cornil (*Soc. Med. de Hôp. de Paris*, xvii. 379) and by Dr. Fereol (*Ibid.*, p. 321).

The absolute demonstration of the degeneration produced by arsenic was, however, made by Dr. Saikowsky (*Virchow's Archiv*, Bd. xxxiv. p. 77), of Moscow, who was also the first to point it out. In his numerous experiments upon rabbits he found that when the animals were poisoned by a small dose of arsenic, so as to live from three to six days, the liver was much enlarged and very fatty,—indeed, contained more fat than the "phosphorus-liver." On microscopical examination, the cells on the exterior of each acinus were seen to be natural; those in the centre in the most advanced stages of degeneration. The kidneys were similarly affected,—their tubes choked up with fat-globules, their epithelium almost completely destroyed. The muscles of the heart and diaphragm were almost equally compromised. Dr. Saikowsky also noted that early in both arsenical and antimonial poisoning the glycogenic function of the liver is abolished.* In frogs poisoned with arsenic the epidermis peels off from the derm, as first noted by Ringer and Murrell, and Emily A. Nunn has found that the influence of the poison is first manifested in the under portion of the epidermis, the degeneration progressing from the derm outwards (*Journal of Physiology*, i. 247).

As arsenic is never used in medicine for an acute effect, the chief interest to the therapeutist centres around its physiological action when given in small doses; yet it seems necessary here to take cognizance of the physiological action of large amounts of the poison.†

Nervous and Muscular System.—The symptoms of arsenical poisoning in man show that the drug has a marked influence upon the nervous system. Dr. W. Sklarek, of Berlin (*Reichert's Archiv*, 1866), has found that the arseniates of potassium and of sodium had exactly the same effect as the arsenic itself upon frogs. Within five minutes after the injection of one-fourth to two c.c. of a two per cent. solution of arsenious acid, or of the arseniates of sodium or potassium, all voluntary movement ceased in the frog; although when the animal was laid upon his back he struggled very actively to recover his position. At this time, however, all sensibility to chemical and mechanical irritants was lost, cutting, burning, or corroding failing to elicit any response. That the motor system was not at fault was shown by the active movements when the frog was placed upon his back, as well as by the results of electrical stimulation of the nerves. The paralysis or quietness must have been due to an abolition of sensation. That this was spinal, and not peripheral, was proven by the circumstance that tying the iliac artery upon one side before the administration of the poison had no effect in preserving sensibility in the protected leg. The only explanation of the struggles of the frog to recover his position after poisoning is to be found in his having been influenced through vision, or else in the theory that the muscular sense is distinct from that of common sensibility and is not affected by arsenic. The researches of Ringer and Murrell (*Journal of Physiology*, i., p. 217) upon frogs have given very different results from those just described, they finding that the symptoms of poisoning came only after the lapse of some hours, and that paralysis of voluntary motion preceded that of sensation and reflex action. Drs. Ringer and Murrell suggest that these differences of result depend upon the time of year at which the frog was experimented on. There is accord between the experimenters in regard to the cause of the final paralysis, all finding that it is produced by a direct action of the arsenic upon the nerve-centres. Ringer and Murrell have also shown, how ever, that the nerves and muscles do not entirely escape the poison, which seems to be more or less toxic to all highly-organized tissues.

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* For a spectroscopic study of the effect of arsenic upon the coloring-matter of the blood, see *Centralblatt*, 1868, p. 609. It is interesting here to note that arsenic, antimony, phosphorus, and ammonia act very similarly, if not identically, upon the blood.

† The theory of Binz and Schulz, that arsenious oxygen acts by taking from protoplasm oxygen, so as to be converted into arsenious acid, and afterwards yields up this oxygen to oxidize the protoplasm, and then repeats the process, seems to me so illy supported, that the reader in regard to it is simply referred to the *Arch. f. Exper. Path. und Pharm.*, xi. 213; xiv. 249; also *British Med. Journ.*, 1882, ii. 1135.

Circulation.—Upon the heart of the frog Dr. Sklarek found that arsenic exerts a very powerful influence, lessening the rapidity and force of the beat, and finally arresting the contraction. That this cardiac action of arsenic is direct was shown by the exact similarity of the phenomena produced by the application of arsenic to the heart cut out of the body. The arrest was never instantaneous, but always preceded by slowing of the beat; and after movement had ceased, galvanic or mechanical irritation caused imperfect systolic movements. In no case did Dr. Sklarek observe any signs of functional excitement preceding the development of the cardiac or motor paralysis.

Dr. Sklarek also found that in arsenical poisoning in the cat there is great reduction in the force and frequency of the heart's pulsations. Recently the effect of the poison upon the circulation of mammals has been elaborately investigated by Dr. S. Unterberger (*Archiv für Exper. Path. und Pharm.*, Bd. ii.). Like Cunza, he found that in arsenical poisoning the heart persists in its movements after the cessation of respiration. Immediately after an injection of the poison in cats and dogs, both the pulse-rate and the arterial pressure fall enormously, and if the dose has been sufficient they never recover themselves. Dr. Unterberger did not make out the cause of the fall of the pulse-rate, but the experiments of Sklarek, already mentioned, indicate that it is due to a direct action on the heart.

The depression of the arterial pressure was shown by Unterberger to be largely due to vaso-motor paralysis, for in an animal under the influence of the poison neither galvanization of a sensory nerve nor of the vaso-motor centre in the upper cord had any influence upon the force of the blood-current. Galvanization of the splanchnics had no effect upon the arterial pressure,—apparently showing that the vaso-motor palsy was peripheral; but Dr. Unterberger found, to his astonishment, that stimulation of the cervical sympathetics had the usual effect upon the vessels of the rabbit's ear. Supposing that these observations be correct, there are only two seemingly possible methods of reconciling them: either the drug acts upon the peripheral vaso-motor nerves in the abdomen, and not upon the same nerves in the neck, or else there is during arsenical poisoning such depression of the power of the cardiac muscle that narrowing of the blood-path does not have the usual effect. Dr. Unterberger found that compression of the abdominal aorta was followed by a great rise of pressure, and therefore believes that the heart in arsenical poisoning has not lost its power. Some complicated transfusion experiments which he made indicated differently, so that whilst his proposition that arsenic paralyzes the peripheral vaso-motor nerves of the abdomen and not those of the head may be considered probable, it certainly is not proven. It would be a very easy matter to decide the question by dividing the spine in a poisoned animal: if the reduction of the arterial pressure be really due to an abdominal vaso-motor paresis, section of the spine should have but little effect on it. There appears to be no doubt that the cardiac muscle is more or less weakened by the poison.

Action of Small Doses.—Minute quantities of arsenic may be given for a long time without producing any perceptible effect, unless it be a sharpening of the appetite, due to the local action on the stomach. When the dose is increased, more active manifestations of gastric irritation may appear, such as loss of appetite, nausea, abdominal pain or uneasiness, diarrhœa, and perhaps sympathetic headache. By the use of frequent small doses these symptoms may be generally avoided, and what may be termed the constitutional action of arsenic be obtained. The first sign of this is generally a puffiness about the eyes, at first visible only in the early mornings, but soon increasing into decided œdema, which after a time may lose its local character and the patient be involved in general anasarca. This anasarca, as was, I believe, first pointed out by Dr. S. Weir Mitchell (*New York Medical Journal*, vol. i.), may or may not be preceded or accompanied by the presence of albumen and of tube-casts in the urine. Beyond the production of the symptoms spoken of, arsenic should never be employed in medicine.

Unfortunately, owing to the frequent use of the metal in the arts, chronic poisoning with it is by no means uncommon.

Although the symptoms vary a good deal and are often obscure, yet in almost every case they are such as should at once awaken suspicion. They have been summed up by Prof. Taylor as follows: "Dryness and irritation of the throat, irritation of the mucous membranes of the eyes and nostrils, dry cough, languor, headache, loss of appetite, nausea, colicky pains, numbness, cramp, irritability of the bowels, attended with mucous discharges, great prostration of strength, a feverish condition, and wasting of the body." It is very evident that the symptoms of irritation of the respiratory mucous membrane are largely, if not entirely, due to the local action of the arsenic, since the poison finds access to the system through the respiratory organs. The constitutional troubles most uniformly present in these cases are weakness and emaciation, often accompanied by more decided nervous manifestations than the picture drawn by Dr. Taylor would suggest: great depression of spirits and irritability of disposition, sleeplessness, giddiness, headache with a feeling of constriction in the forehead, numbness in the extremities, muscular tremors or stiffness, vertigo, and even convulsions and paralysis, are very common. Indeed, in some cases these nervous symptoms constitute the chief if not the sole features. (See *Deutsches Klinik*, 1874, No. 31; also *Schmidt's Jahrbücher*, Bd. clxv. p. 233.)

Dr. Kirchgässer, as the result of very large experience, asserts that the most characteristic phenomena of chronic arsenicism are a brown pigment-deposit in the skin of the face, inflammatory affection of the eyelids, and the disturbances of sensibility and motion, which affect most frequently the lower extremities, together with scalding during urination. Out of eight cases, he found arsenic in the urine in six (*Berlin. Centralblatt*, p. 574, 1868).

Seemingly opposed to this every-day experience is the asserted "arsenic-eating" of the peasants of Styria. It is stated by some that the arsenic is taken by the young girls to beautify their complexion and to enhance their charms; by others, that the object sought to be attained is protection against arsenical fumes by those engaged in the manufacture of the metal, and the increase of the powers of endurance and of the "wind" in huntsmen and others who do a great deal of mountain-climbing. The habit is said not to be detrimental to life. Indeed, the toxiphagi are asserted to be remarkably long-lived people. In regard to the dose, three grains are said to be taken as a commencement, and to be increased to thirty! Originally affirmed by Vogt (*Lehrbuch der Pharmacodynamik*, dritte Aufl., Bd. i.), the existence of this practice has been especially asserted by Tschudi (quoted by Prof. Stillé), and more recently by Chs. Heisch (*Pharmaceutical Journal and Transactions*, vol. i., 2d series, 1859 and 1860, p. 556).

Notwithstanding the assertion of Heisch, the existence of the practice was not credited (see *British and Foreign Med.-Chir. Review*, vol. xxix. p. 144), but in 1864 Dr. C. Maclagan (*Edin. Med. Journ.*, 1864, p. 203) visited Styria, saw several arsenic-eaters, administered to one of them five grains of the substance at a dose without ill effects, and found the poison in the urine He also analyzed the material which the men habitually took, and found it to be arsenic.

An unsigned (editorial?) communication in the *Edinburgh Medical and Surgical Journal* (1871, vol. xvi. p. 569) further asserts that a royal commission has examined into the subject, and that their report indicates that the practice exists, but that it has been grossly exaggerated. They affirm that arsenic-eating is practiced chiefly in the northern and northwestern parts of Styria; that the white arsenic is preferred, the yellow commercial article being sometimes taken, the native red arsenic, or orpiment, very rarely; that the commencing dose is about 0.22 grain, which is very slowly increased to 0.62 grain avoirdupois. The "ratsbane-eaters" almost all belong to the lower classes, and are said to be generally strong and healthy persons, courageous, pugnacious, and of strong sexual disposition. These statements are in accord with those of Dr. Maclagan, and must, I think, be accepted as true. Dr. Maclagan also says that in one case of suspected murder in Styria the prisoner was acquitted on the ground that the deceased was an arsenic-eater.

Of especial interest in connection with arsenic-eating is the verity or non verity of the asserted effect of the drug upon tissue-changes. Schmidt and Stürzwage believe that it has such action in a very marked degree, because in their experiments upon rabbits they found a decided diminution in the excretion of carbonic acid and of urea during the use of minute doses of the poison. Fokker (*Schmidt's Jahrb.*, clviii. 13), however, was unable to perceive in three experiments that daily doses of from .15 to .075 grain of arsenic to a dog had any effect upon the elimination of urea, and Kossell and Gaethgens, in two experiments, have noted a very decided increase of the elimination of urea produced by toxic doses of arsenic in the dog (*Arch. Exper. Pathol. et Pharm.*, Bd. v. 133, also *Centralb. Med. Wissen.*, 1875, 530; 1876, 833). At present the evidence is not sufficient to warrant a positive opinion, but appears to indicate increased nitrogenous elimination as the result of repeated small toxic doses of arsenic.

When arsenic is administered in small repeated doses, it may act as a tonic, by slightly irritating the stomach and thereby provoking an appetite · and in certain cachexias it does increase the muscular strength and the general vigor. The history of arsenic-eating indicates that the drug has some positive tonic influence over nutrition, and although the amelioration, the increase of strength and blood, by its use in cachexias may be due to an indirect action of the drug,—to a removal or overcoming of the morbific agent on the disease, and a consequent allowing of the recuperative powers of the system to assert themselves,—there is much reason for believing that it acts largely as a direct stimulant to nutrition. All that we know of the effect of arsenic upon the system throws only enough light upon its therapeutic action to enable us to class it as an alterative,—a modifier and often an improver of nutrition.

Elimination.—There is abundant proof of the absorption, and no less of the elimination, of arsenic. Indeed, the latter appears to take place with exceptional rapidity. Thus, MM. Flandin and Danger (Husemann, *Toxicologie*, p. 823) failed, three days after the last dose, to detect it in the bodies of animals to which fifteen grains had been given daily; and in a child killed in two days by an arsenical pigment, none of the metal could be found in the body (*British and Foreign Med.-Chir. Review*, 1870, vol. xlv.). In the great majority of instances, however, there is no trouble in finding arsenic in the bodies of those poisoned by it, and Steinhäuser reports a case in which it was found in the remnants of a corpse that had been buried for twenty-two years (*Berlin. Centralblatt*, 1868, p. 160). The principal channel of escape is the kidneys; but elimination also takes place through the mucous membrane of the alimentary canal, through the skin, and even in the saliva and the tears. Unterberger has detected it in the alimentary canal of animals poisoned by injection into the vein. M. Chatin has found it in the serosity of a blister, Bergeron and Lemaître in the sweat (*British and Foreign Med.-Chir. Review*, vol. xlviii., 1871), and Taylor (*Guy's Hospital Reports*, vol. x., 3d series, 1864, p. 227) in the contents of the stomach of a child poisoned by its application to the scalp.*

Especially in connection with the therapeutic use of arsenic in malarial fever, some interest attaches to the effect of the drug upon the lower organisms and fermentations. The subject has been partially investigated by Johannsohn (*Arch. für Exper. Path. und Therap.*, Bd. ii. p. 106), who concludes that the poison produces a peculiar degeneration of the yeast-plant, but actually increases the production of bacteria in yeast. When small amounts of arsenic were added to yeast and syrup, the fermentative process was at first very much checked, but not absolutely prevented. After a time the process went on faster again. In urine Johannsohn found that the poison hindered the production of Micrococcus urea, but actually favored that of other fungi. In the lactic fermentation the growth of the peculiar fungi was checked, whilst that of Mucor mucedo was favored. The fact that arsenic acts slowly upon the yeast has been confirmed by Schaefer and Boehm (*Arbeiten Physiol. Inst. Würzburger Hochschule*, 1873, p. 173). Both Johannsohn and Schaefer and Boehm have found that arsenic exerts no influence upon non-organized ferments, either vegetable or animal, such as amygdalin, pepsin, pancreatin, etc.

THERAPEUTICS.—Our knowledge of the value of arsenic in disease rests solely upon clinical observation, which has abundantly established its use in certain very diverse affections. Chief among these is *chronic malarial dyscrasia*. No one would at present think of employing it in acute *remittent fever*, or even in acute *intermittent*, unless under very peculiar circumstances. It is in those cases which have resisted quinia, in which the paroxysms have become irregular, returning at long or irregular intervals, and in which the anæmia and the general nutritive disturbance are even more prominent than the febrile disorder, that arsenic is especially valuable. In these cases it should be administered with sufficient boldness, very generally in conjunction with iron. Prof. George B. Wood recommends that the first doses should be as large as the system will endure, so as to make a decided impression at once. When the ague-paroxysms are frequent, it is perhaps well to employ this plan; but when it is rather the cachexia than the active disorder that is to be combated, it is preferable to commence with small doses and to increase them until some constitutional symptom is produced. In ordinary *intermittents*, after the paroxysms have been broken up by quinine it is very well to place the patient upon a preparation of arsenic, iron, and quinine, as a prophylactic against their return. When, in ordinary *intermittent* fever, for any cause quinia cannot be administered, arsenic may be employed. In these cases, as already intimated, the first doses should be large, so as to make an immediate impression; from five to ten minims of Fowler's solution, properly diluted, may be given every two or three hours until some decided symptom is produced. When the stomach refuses the remedy, it has been recommended by Boudin to give it by the rectum, which he affirms will often bear even a grain of the acid. Not more than a third of this amount should, however, be used as a commencing dose. In *malarial intermittent neuralgia*, arsenic may be employed as a very useful adjuvant to the antiperiodic alkaloids. Dr. K. M. Downie calls attention (*Indian Medical Journal*, 1872) to the value of arsenic as a *prophylactic* against malaria. His trials were not numerous enough to be conclusive, but so far as they go they indicate that arsenic is even superior to quinia. Recently attention has been drawn to the great value of arsenic in *lymphatic tumors*, especially in the affection known as malignant *lymphoma* (*Wien. Med. Woch.*, 1871; *Arch. Klin. Chir.*, xviii.; *Stricker's Jahr.*, 1877). Advantage is said to be sometimes derived from injections of the remedy into the growth.

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* Various observers have endeavored to determine which tissues contain most arsenic after death from the poison, with varying results. Consult *Arch. d. Physiol. Norm. et Path.*, 1875, ii. 653; *Chem. Centrallblatt*, 1879, 602; *Arch. Exper. Path. u. Pharm.*, xiii. 257; *The Chemist and Druggist*, xxi., 1879, 381; *Comptes-Rendus*, 1879, lxxxviii. 1212.

Having had very little experience myself in the use of arsenic in *skin disease*, Dr. Louis A. Duhring, Professor of Dermatology in the University Hospital, has kindly furnished me with the following:

As is well known, arsenic has long been used and held in high esteem as a remedy in the treatment of cutaneous diseases. It is proper to state, however, that at the present day there exists a great diversity of opinion concerning its actual value as a therapeutic agent against this class of diseases. Certain dermatologists claim to derive marked good from its employment in quite a large number of affections, while others of equal experience are inclined to place but little reliance upon its curative powers. Without entering at all into this discussion, it may be unhesitatingly said that it is a remedy of real worth and service in several very important cutaneous diseases, and that it may be combined with other remedies and used with good result in certain other diseases of the skin, acting in these cases as a general tonic. It is the dermatologist's most valuable internal remedy in a large number of cases. But it must be skilfully employed, and the cases, moreover, must be selected if we would expect satisfactory results. To say that arsenic is of use in diseases of the skin viewed collectively, is an assertion so vague as to be of no practical value. Not only is it necessary to specify the disease, but it is even important to designate the particular stage if we would employ the remedy successfully.

Arsenic exerts its influence chiefly upon the epidermis. Hence it is found that diseases affecting the more superficial strata of the skin are most amenable to its influence. It possesses little or no effect upon the diseases which have their seat in the deeper structures.

Its action upon the skin is slow, weeks and months being requisite to produce the desired result. Improvement once obtained, it is usually expedient to allow the patient to continue the use of the remedy for some weeks after all symptoms of the disease have disappeared.

Arsenic should never be employed in the acute, inflammatory stage of any disease of the skin. It should not be prescribed when there is great heat, burning, intense itching, or rapid cell-change. It not only is of no benefit at this stage, but is in most cases positively injurious, tending to augment the activity of the morbid process. It stimulates the rete into action when rest is most needed. Its administration should be withheld until the acute symptoms have subsided.

Of many of the dissimilar diseases in which arsenic has been employed, both with and without reputed success, no mention need here be made. It will suffice for the purpose in hand to refer to those affections which it is generally conceded are more or less favorably influenced. It is unquestionably of great value in *psoriasis*. But it is not of benefit in every case, nor should it be prescribed for all forms, or in all stages, of this disease. When the process is very active, attended with intense hyperæmia, arsenic, as a rule, only aggravates the inflammatory condition. The more active the cell-proliferation, the less probability is there of its being of benefit. On the other hand, the more indolent and sluggish the disease, the greater the chances for improvement. It should be withheld until the process has fairly settled in its career. In cases of psoriasis of long standing, which manifest little disposition to undergo change, it is particularly useful.

It is of undoubted service in certain varieties of *eczema*, especially in the chronic squamous and papular varieties; also where the elementary lesions are but ill defined; and, finally, where the disease is unusually superficially seated, and where there is only slight infiltration of the skin. Certain forms of persistent localized papular and vesicular eczema, having a marked tendency to recur, as, for example, of the fingers, also often yield readily to arsenic. It should, of course, be avoided in acute eczema.

Pemphigus is decidedly influenced, and often permanently relieved, by its use. It is our most reliable remedy for this disease. Here, as in other conditions, the older the process the more likely are we to obtain favorable results. In *lichen planus* and in *lichen ruber* it is employed with great advantage. Prescribed in minute doses, as a tonic, it may sometimes be given with benefit in chronic *urticaria*.

It is likewise of value in certain varieties of *acne*. Before prescribing it, however, the digestive tract should be carefully looked into, and if disordered in the least degree, it should first be rectified. The same remark holds good for its use in all diseases of the skin. Taken for a considerable time, several months, it often exerts a marked influence upon the small pustular and papular forms of acne, and also in those cases where there is an accompanying erythematous rosacea.

The two preparations of arsenic which it is, as a rule, advisable to employ are arsenious acid and liquor potassii arsenitis. The latter will be found the more desirable form for ordinary use. Arsenious acid is given in pill form, with sugar of milk, or combined with a grain each of black pepper and powdered liquorice, constituting the compound known as the Asiatic pill, which may be prescribed in various strengths, suitable to the case. The liquor potassii arsenitis is best given with water or combined with a bitter tincture or infusion; it is also well borne combined with the wine of iron. The mode of ordering the solution pure, and directing so many drops to be taken at each dose, is, in my opinion, objectionable for many reasons, to which it is unnecessary to refer. The average dose suitable to the majority of individuals is three minims. Smaller doses, one or two minims thrice daily, are often demanded, and in many cases are found to be much more beneficial than larger doses. On the other hand, four, six, or eight minims will not infrequently be tolerated, and occasionally even larger doses; but out of a number of patients it will be found that but few can take more than three or four minims for any length of time without derangement of the system. Arsenic should always be taken either with the food or directly afterwards.

In certain nervous affections arsenic acts very favorably, in some unknown way. It is especially in *chorea* that it has acquired a deserved reputation. In this affection iron and other tonics are generally indicated, and may be given consentaneously with the arsenic. It is best, however, to administer the latter separately, as the dose must be steadily increased until œdema or other manifestations betray its decided action. Arsenic has also been recommended in *whooping-cough*, but is at present very rarely, if ever, used. In ordinary *non-malarial neuralgia* it may be tried, and is sometimes serviceable; in simple *gastralgia*, or *gastric neuralgia*, it has been especially recommended.

Arsenic is employed sometimes with advantage in *asthma*, and may be given by the stomach, but is perhaps more generally useful when inhaled. The following formula has been long employed in the Philadelphia Hospital. The prepared paper is rolled into cigarettes, one of which is smoked two or three times a day, until relief is afforded or some giddiness produced:

CHARTA ARSENICALIS COMPOSITA (*Compound Arsenical Paper*). ℞—Belladonnæ fol., gr. xcvi; hyoscyami fol., stramonii fol., āā gr. xlviii; extr. opii, gr. iv; tabaci, gr. lxxx; aquæ, Oj; M., ft. sol. et add. potas. nit., gr. clx; potas. arsenit., gr. cccxx. Saturate bibulous paper and dry for use.

Arsenic is of value in those forms of *chronic rheumatism* in which iodide of potassium is commonly employed. It is often advantageous to alternate, administering one of these alteratives for three or four weeks, and then the other for the same length of time. In *rheumatic gout*, or *rheumatoid arthritis*, it has been highly extolled, but in my experience has furnished no better results than other remedies. It should, however, always be tried in this most obstinate disorder.

There has been quite a number of cases reported in which an outbreak of Herpes Zoster has occurred during the long continued use of arsenic, and it does seem as though the arsenic was the cause of the eruption. (For paper, giving cases and bibliography, by O. Juliusburger, see *Vierteljahr. f. Dermatol. Wien.*, xi. 97.)

TOXICOLOGY.—Sufficient has already been said concerning the symptoms of both acute and chronic arsenical poisoning. No mention has, however, been made of the peculiar local affections produced in the hands of those artisans who work with the preparations of arsenic. Ulcers about the roots of the nails are generally the first trouble in these cases, but after a time eczematous or papular eruptions appear, and even subdermal erysipelatous inflammation is developed. Very commonly to these local symptoms are added, after a time, the usual phenomena of chronic arsenical poisoning.

In the arts, preparations of arsenic are largely used as pigments;* and, excepting the manufacturers of arsenic, it is almost exclusively those who are accidentally exposed to the deleterious influence of these pigments who suffer from chronic arsenical poisoning. The poisonous colors are all of some shade of green, and, being very cheap, and remarkable for their purity of tone and their permanence under exposure to light, are much used by paper-makers. Scheele's green—the arsenite of copper, contains fifty-five per cent., by weight, of arsenious acid; and Schweinfurt green—the aceto-arsenite—fifty-eight per cent. Paper coated with them has been largely used not only as hangings, but even as wrappings for confectionery and other edibles. Sweetmeats have been colored with them; pasteboard boxes, artificial flowers, tarlatan dresses, shelves in groceries, walls of dwellings, toys of children, and various other articles, have been made the vehicles of death, so that hundreds of cases of poisoning more or less severe have resulted from the use of these pigments, which ought to be banished by the strictest laws. In most cases it is probably the minute dust, which is separated mechanically and diffused through the room, that produces the fatal result; but poisoning has occurred when the arsenical paper was covered over with another paper. Dr. Hambers has made elaborate chemical researches upon the air of these apartments, and believes that he has demonstrated that some arsenic escapes in the form of arseniuretted hydrogen. Not rarely the poison has been taken directly into the stomach, especially by children.

The time at which death occurs as well as the fatal dose of arsenic varies very much. Death usually results in from eighteen hours to three days; but Taylor reports a case in which it occurred with tetanic symptoms in twenty minutes, and life has been protracted until the sixteenth or even the twentieth day. Dr. W. C. Jackson (*Amer. Journ. of the Med. Sciences*, July, 1858) reports a case of recovery, under the early use of emetics, after an estimated dose of two ounces had been taken; and Dr. E. D. Mackenzie gives an account (*Indian Medical Gazette*, 1872) of a man who swallowed an unknown quantity of arsenic in lumps, and received no treatment for sixteen hours, yet recovered after passing per anum one hundred and five grains of arsenic in two masses. On the other hand, death has resulted from the use of very small amounts. Dr. Taylor asserts that the smallest fatal dose hitherto recorded is two grains. Dr. Lachèse (*Ann. d'Hyg. et de Méd. Légale*, 1834, 1e sér., t. xvii.) affirms that six milligrammes (0.09 gr.) will produce decided but not serious symptoms, and that from one to three centigrammes (0.154 to 0.462 gr.) are poisonous, and from five to ten centigrammes (0.77 to 1.54 gr.) fatal. Tardieu places the minimum lethal dose at from ten to fifteen centigrammes (1.54 to 2.31 gr.). The escapes from death after the ingestion of large amounts of arsenic have, without doubt, depended upon its being, as in the cases above narrated, in an insoluble form. The effects of the arsenical solutions, such as Fowler's, are more rapid and severe than those of the solid drug.

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* For an excellent report upon this subject, see *Report of the State Board of Health of Massachusetts*, Jan. 1872, where it is stated that from five hundred to seven hundred tons of arsenical pigment were manufactured in 1862 in England alone. Fatal chronic arsenical poisoning from working in aniline dyes is reported in *Stricker's Med. Jahrb.*, 1877, 501

As arsenic in large doses generally induces vomiting, it is very rarely necessary in poisoning to evacuate the stomach by artificial means. If free emesis, however, have not occurred, a prompt emetic, such as mustard or sulphate of zinc, should be at once exhibited, and very generally the stomach should be well washed out by large draughts of warm water, with salt, if necessary for the return of the water. With the emetic, or sooner, if possible, the antidote should be administered. The substance whose antidotal value has been most thoroughly tested and assured by clinical experience is the *freshly precipitated sesquioxide of iron*, which forms with arsenious acid a very insoluble compound. The antidote must be freshly prepared, and must be given in great excess: according to the experiments of Messrs. T. and H. Smith, of Edinburgh, at least eight grains of the iron being required for the conversion of one grain of the arsenious acid. In practice, any of the sesqui solutions of iron—that of the chloride being generally preferred, as most readily procured—should be neutralized by the carbonate of sodium, and a portion of the precipitate given at once, stirred up in *hot* water. The remainder of the antidote, having been hastily washed by emptying on to a piece of muslin or a filter, pouring water on it and allowing it to drain, should be administered very freely,—indeed, indefinitely, as it is entirely harmless. Recently, H. Köhler, of Halle (*Brit. and For. Med.-Chir. Rev.*, 1870, vol. xlv. p. 538), has made a very elaborate series of chemical, physiological, and clinical experiments upon the comparative antidotal values of the *saccharated oxide* of iron and the freshly-precipitated sesquioxide. His results indicate that the former preparation is the better; but, as the efficiency of the sesquioxide has been so frequently proven at the bedside, further testimony is desirable before it is superseded, especially since the other ferric preparation is not officinal with us, and is not so readily prepared on the spur of the moment as its fellow. *Dialyzed Iron* has been used with very good results, but it is much better to precipitate it, just before administration, with a small amount of ammonia or other alkali. *Magnesia*, freshly calcined or freshly precipitated from a solution of its salts, is an antidote of some avail in arsenical poisoning, but is decidedly less efficient than the oxide of iron.

After the emetic has acted in a case of arsenical poisoning, and while the antidote is being given, castor oil should be administered, for the purpose of expelling the poison from the bowels. The further treatment should be directed by general principles: demulcent drinks, opium, stimulants, dry external heat, and rubbing, being employed as called for by the symptoms. When there is a tendency to suppression of urine, very large draughts of water containing sweet spirits of nitre should be given as frequently as the stomach will bear them.

The chief indications in *chronic arsenical poisoning* are to remove the patient from the exposure and to treat symptoms as they arise. Although I do not know of any clinical records bearing upon the subject, it might be well to exhibit the iodide of potassium, with the hope of hastening the elimination of the poison.

ADMINISTRATION.—The commencing dose of arsenic is one-twentieth of a grain, which should be given in pill *after* meals, and be slowly increased until a perceptible influence, or the desired therapeutic effect, is obtained. In many cases (chorea, lymphoma, intermittent fevers, etc.) it is necessary to push the remedy until decided evidences of poisoning are secured; in this case a liquid preparation should be selected. The following are the U. S. P. preparations of arsenic:

Liquor Potassii Arsenitis—Solution of Arsenite of Potassium.—Fowler's Solution contains four grains of arsenious acid to the ounce, is nearly colorless, odorless, with a very faint taste of the compound spirit of lavender, which is in it. It is an excellent preparation. The average commencement dose is five drops in a wineglassful of water after meals, to be increased and used with the same precautions as arsenic.

Sodii Arsenias—Arseniate of Sodium.—This salt occurs in transparent, slightly efflorescent, soluble crystals, and is solely used in making the *Liquor Sodii Arseniatis.* The *Solution of Arseniate of Sodium* (gr. 4.6 to f℥i) may be used instead of Fowler's Solution, in similar doses.

Arsenii Iodidum—Iodide of Arsenic.—This is an orange-red, crystalline solid, wholly soluble in water and entirely volatilized by heat. It has been used as an alterative, and also as an external application in certain diseases of the skin, especially *lupus* and *chronic tubercular affections.* Iodide of arsenic enters into *Donovan's Solution.*

Liquor Acidi Arseniosi—Solution of Arsenious Acid, is of the same strength, and has the same therapeutic properties, as Fowler's Solution. It is, however, a little more irritant than that preparation.

HYDRARGYRUM—MERCURY. U.S.

Physiological Action.—When a mild, unirritating preparation of mercury is introduced into the system so as to produce constitutional effects, the first symptoms of its action are to be looked for in the mouth. In the mildest degree these symptoms consist of a slight fetor of the breath, and some soreness of the teeth when knocked forcibly together or struck with a key. Mercurial fetor is peculiar, and is generally the first indication that the drug is affecting the system, and is sooner or later accompanied by a disagreeable metallic taste. If the use of the mercury be persisted in, the gums become swollen, soft, and spongy, bleeding on very slight abrasion, and there is a decided increase in the secretion of saliva. Beyond this point the therapeutist is never justified in carrying the use of the drug. If it is done, the local symptoms in the mouth increase in severity, the gums become swollen, inflamed, very vascular, and marked by a dark-red line at the junction of the teeth; the tongue is also swollen, sometimes enormously, protruding from the mouth, whose closure it may entirely prevent; the teeth are loosened in their sockets; the saliva is enormously increased in quantity and altered in quality, forming great, ropy, viscid masses, which pour over the thickened lips; the parotid glands, and even the submaxillary, are very much enlarged, and tender. Sometimes, before salivation occurs, slight systemic erethism, marked by a quickened pulse and general restlessness, may be present; but when the mouth-symptoms are severe, very generally there is a distinct febrile reaction of a low type.

In some cases of mercurialization the stomatitis has been very intense. loss of the teeth, extensive ulceration of the soft parts, and even necrosis of the jaw-bones, have occurred, and death from exhaustion resulted, or the patient struggled through to recovery, seamed and disfigured for life. In these cases passive hemorrhages often recur again and again, and, it may be, contribute largely to a fatal result. During severe ptyalism emaciation goes on rapidly, and seems to affect especially imperfectly organized tissues, so that exudations very generally rapidly disappear. The disturbance of nutrition is further shown in some cases by the occurrence of ulcers upon the extremities. The blood suffers very decidedly, becoming more fluid and watery than normal, and having its power of coagulation impaired. According to the researches of Dr. Wright, its solid constituents are notably diminished, including albumen, fibrin, and the red corpuscles, and it contains a large quantity of a fetid, fatty material. These observations of Wright have been confirmed upon animals by Dr. Wilbouchewitch (*Arch. de Physiol.*, Sept. 1874), and by Dr. I. Hughes Bennett.

Although large doses of mercury lower the general nutrition and destroy the crasis of the blood, it is by no means certain that given in very minute doses it has not tonic properties. In 1869 (*Gaz. des Hôp.*) Liègrois asserted that the subcutaneous injection of very minute doses of quicksilver produces in healthy men an increase of their bodily weight, and in 1876, in two experiments, Dr. E. L. Keyes (*Amer. Journ. Med. Sci.*, Jan. 1876) found that not only was the bodily weight increased, but, as determined by actual count, the number of the red corpuscles very decidedly augmented. Very recently (*Arch. Exp. Path. u. Pharm.*, Bd. xiii. 317) Dr. Hermann Schlesinger has laboriously experimented upon rabbits and dogs. All other conditions being similar, those rabbits which received the mercury increased in weight a very little more than did those to which mercury was not given, but the augmentation of the red blood-disks was decidedly greater in the mercurialized animals. With dogs the results were more decided, both bodily weight and blood-corpuscles increasing much faster in the animal to which mercury was given. Prof. I. Hughes Bennett had previously obtained similar results to those quoted, and Dr. Schlesinger thinks that it must be considered proven that very minute continuous doses of mercurials tend in the normal animal or man to distinctly increase the weight of the body and the richness of the blood, but that it is scarcely proper to call them tonic, as in his belief they act by hindering oxidation and restricting waste, and not by aiding in reconstruction. In this, however, he seems resting upon theory rather than upon proven fact, and there is much clinical reason for believing that in exceedingly minute doses mercurials in some way benefit nutrition.

Sometimes the influence of mercury falls almost exclusively upon the nervous system, and produces a peculiar train of paralytic phenomena. This occurs chiefly, if not exclusively, when it, as vapor, finds entrance to the blood through the lungs, and is most frequently seen in those who work in the metal. It is generally the result of long exposure; but that it may be produced in a very short time is proven by the case, related by Dr. Christison, of two barometer-makers who slept one night in a room containing a pot of mercury upon a stove. One was severely salivated, the other was affected with a shaking palsy which lasted all his life. According to Dr. Sigmond (*Mercury, Blue Pill, and Calomel*, London, 1840), the attack of mercurial palsy, which is sometimes sudden, sometimes gradual, begins with unsteadiness and shaking of the extremities, and of the muscles of the face, which movements interfere with walking, speaking, or chewing; the tremors become frequent, nay, almost constant; "every action is performed by starts." If the exposure be continued, sleeplessness, loss of memory, and death terminate the scene. A peculiar brownish hue of the whole body, and dry skin, generally accompany the disease. In its first attack it may be mistaken for St. Vitus's dance; in its latter stages, for delirium tremens. According to Noël Guéneau de Mussy (*Gazette des Hôpitaux*, 1868), these two forms are rather distinct varieties than different stages of mercurial tremors. In the latter the affection simulates *paralysis agitans* in its shaking movements; in the former the motions are violent, and occur independently of the will of the patient, even when he is lying quietly in bed. In a case reported by Dr. L. Langer, the electro-contractility of the affected muscles was much heightened (*Wien. Med. Jahrb.*, 1881, 478).

In other cases, neuralgic pains are a prominent result of mercurial exposure; and sometimes epilepsy is produced, or the intellect is especially affected, and insanity, most frequently of a melancholic type, results. According to Dr. Sigmond, the peculiar paralysis of lead-poisoning, including the drop-wrist, has been known to follow persistent mercurial inunctions.

In some cases, exposure to the vapor of mercury, or even its persistent medicinal use, has resulted in the production of a state of the system somewhat resembling scurvy, characterized by great anæmia, emaciation, and general loss of power, with loss of the hair, aching pains in the bones and joints, œdema, fetid breath, diarrhœa, and, generally, disordered secretions. This is the so-called *mercurial cachexia.*

As already stated, the salivary glands are especially sensitive to the constitutional effects of mercury, and there is some reason for believing that the pancreas, which resembles them in structure, is also obnoxious to the drug. Thus, in a case related by Dr. Copland, a woman after excessive salivation experienced deep-seated epigastric pain and heat, with nausea, thirst, and fever, and voided thin stools containing liquid resembling salivary fluid. At the post-mortem the pancreas was found weighing four ounces, red, congested, and with its duct dilated. In regard to the action of mercury upon the liver, see article on Calomel as a purgative.

It is asserted that in some peculiar persons the external, and even the internal use of small amounts of mercurials will produce violent eczema or other skin eruption (Dr. Alexander, *Vierteljahrs. f. Dermatol. u. Syph.*, xi. 110).

No attention has, that I am aware of, been paid to *local mercurial* poisoning, but Dr. A. W. Foot has reported (*Dublin Journ. of Med. Sci.*, 1873) a case in which paralysis of the muscles of the hand and fore-arm was produced by contact with the red iodide of mercury during the rubbing of cattle with a salve containing it.

That mercury is absorbed there is abundant proof.* That it is eliminated by the secretions is also very evident. Thus, it has been found in the blood,† in the urine,[*] in the serum of ulcers,[†] in the saliva,[‡] in the fæces,[§] in the pus from ulcers, in the seminal fluid,[‖] in the milk of nursing women,[¶] indeed, in every conceivable secretion and in every tissue. Heller, of Vienna,[**] has found it in the aborted fœtuses of salivated women, and Mayençon and Bergeret in the urine of a baby whose nurse was taking calomel.

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* Dr. S. V. Clevenger (*Chicago Med. Gaz.*, Feb. 20, 1880) believes that mercurials are absorbed, and act in the form of excessively minute globules of the pure metal. Many of his statements are absurdly extravagant, but his observation that when calomel is given to a chicken the metallic globules can be abundantly seen in the blood should be confirmed or overthrown by direct experiments. See also *Chicago Med. Gaz.*, 1880, i. 155.

As N. Popow found that mercury is capable of producing the same changes in the spinal cord as is arsenic (see p. 410), it is probable that in some cases of mercurial poisoning the symptoms simulate those of poliomyelitis.

† Eld and Buchner, quoted by Prof. Stillé.

It is a matter of much interest to know how rapidly mercury is eliminated, and whether, when given internally, it accumulates in the system. The recent researches of Mayençon and Bergeret (*loc. cit.*) throw some light upon this point as well as upon the rapidity of absorption. They found that if one centigramme of corrosive sublimate was given hypodermically to a dog, the urine for the next twenty-four hours contained mercury, afterwards none. When a centigramme was given daily for ten or twelve days, the urine contained mercury for four or five days after the cessation of medication. In their last series of experiments, rabbits received the drug, and were killed at different intervals: in half an hour the metal could be found in all the tissues, the liver and kidneys containing most of it; in four days, or even in a shorter time, mercury given in a single dose was all eliminated, and could not be found in the tissues. This would seem to prove that mercury given in a single dose does not remain in the system; but the experiments of Mayençon and his colleague, confirmed by clinical experience, show that when the drug is administered repeatedly elimination ceases before it is all discharged. Thus, forty-eight hours after the cessation of a mercurial course, when the urine of one of the investigators was free from the metal, the iodide of potassium was exhibited; and the urine of the next twenty-four hours contained an abundance of mercury, which continued to be present in diminishing quantities for seventy-two hours. The chief channel of escape seems to be the kidneys; but it is very certain that, at least in some cases, the drug is freely excreted by the salivary glands as well as by the intestines. Dr. Schuster has found it in the fæces three months after the cessation of a mercurial course (*Viertelj. f. Dermat. u. Syphilis*, ix. 307); indeed, he believes that it is thrown off more freely and constantly by the intestines than by the kidneys. He also claims that elimination is completed six months after the cessation of an ordinary mercurial course (*Journal of Cutan. Med.*, i. No. 12, ii. No. 9).[††]

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[*] Cantu, Jourda, Andouard, quoted by Prof. Stillé.

[†] Fourcroy, quoted by Prof. Stillé.

[‡] Gmelin, *Bull. de Thérap.*, xiii.; Bynnon, quoted by Mayençon and Bergeret; Saikowsky, *Virchow's Archiv*, xxxvii. 347; Oesterlen, quoted by Prof. Stillé.

[§] Saikowsky, *loc. cit.*, p. 347.

[‖] Mayençon and Bergeret, *Robin's Journal de l'Anatomie*, 1873.

[¶] Klinik, *Detroit Med. Journ.*, May, 1877.

[**] Quoted by Prof. Stillé.

[††] These papers of Schuster have given rise to some controversy, and a valuable discussion as to the best methods of finding mercury in the excreta. See papers quoted above; also *Viertel̆jahrs. f. Dermatol. u. Syph.*, 1882, No. 702; *Annal. de Dermat. et Syphil.*, iii. 1882, 721. Sigismund has found quicksilver in the urine of patients as long as thirteen

In regard to the constitutional action of mercury we know but little, except that in some way it influences nutrition.* It certainly increases the secretions, probably by a direct action upon the cells of all the glands. It has been shown by Salkowsky that mercury will cause in the dog fatty degeneration of the renal epithelium, and in the rabbit diabetes, as well as a deposit of the phosphate of calcium in the kidneys, which Prof. Prevost has shown to be accompanied with a decalcification of the bones (*Revue Méd. de la Suisse Rom.*, 1882, 553, 605; also 1883, 402). These facts, and the emaciation, the perverted functions of nerves and glandular tissue, the various skin-eruptions, the altered blood of chronic hydrargyria, all point to a profound impression on the nutrition of every part of the organism.

That mercury causes no especial waste or destruction of the nitrogenous compounds of the body appears to be shown by the researches of Dr. Hermann von Boeck (*Schmidt's Jahrbücher*, Bd. cxlv. p. 142). This observer analyzed the fæces and urine of a man before, during, and after the exhibition of mercury, taking proper precautions to assure uniformity as to diet and exercise. There was a slight but not a notable increase in the amount of nitrogen in the two excretions during the mercurial period.

THERAPEUTICS.—The use of mercury in affections of the liver and of the alimentary canal is fully discussed in another portion of this work; and, although the drug has been used for almost innumerable purposes in times past, it seems here only necessary to speak of its action as an antiphlogistic and as an antisyphilitic.

Antiphlogistic action.—The use of mercury in inflammation originated towards the close of the last century with a Dr. Robert Hamilton, and soon became universal in England and America. It is a matter of regret that no sufficient analysis of the blood of ptyalized persons has been made to determine exactly what are the changes produced in the vital fluid by mercury. The indications are, however, very strong that chief among them is a lessening of the amount of fibrin. As is well known, increase of the hæmic fibrin is one of the most characteristic effects of inflammation: consequently, theory, so far from being opposed to the antiphlogistic use of calomel, affords at least some grounds for the belief that there is more or less of antagonism between the processes of mercurialization and of inflammation.

All important evidence as to the antiphlogistic value of mercurials at

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years after taking the medicine; but Schuster (*Zeitschr. f. Klin. Med.*, vii. 1884) asserts that these patients were habitués of a room in which inunctions were constantly being made, and that under these circumstances there is sufficient diffusion of the mercury to produce a very sensible effect in those breathing the air.

* For an article by A. Polotebenow, of St. Petersburg, on the effect of mixing corrosive sublimate albuminate with blood outside of the body, see *Virchow's Archiv*, 1864, Bd. xxi. p. 35. Mercury acts upon the lower mammals as it does upon man, but experimental research has as yet thrown little light upon the method of its action. For the latest research and literature of the subject, see *Archiv Exper. Path. und Pharm.*, xiii. 86.

present available is clinical, and even of this it seems impossible to find much that is very exact and of such nature as to exclude possible fallacies. It is the enormous mass of testimony that overrides the chance of fallacies. It is the general judgment of the profession, founded upon the thousand daily-observed bedside facts, that indorses the use of mercury as an antiphlogistic. In other words, our knowledge of the value of mercurials in inflammation at present is clinical rather than experimental, empirical rather than scientific, but it seems scarcely possible that it is not correct. There is one inflammatory affection, *iritis*, which, from its anatomical relations, is completely visible at all stages; and the effects of the drug upon its processes have been noted from day to day hundreds of times. Oculists are, I believe, agreed that when there is a marked tendency towards the exudation of lymph in this disease, mercury is to be exhibited until ptyalism is induced.

Of all inflammations, those of the *serous membranes* seem to be most allied to iritis; and it is exactly in the condition above spoken of, where there is a tendency to fibrinous exudations in *pleuritis*, *peritonitis*, and *pericarditis*, that mercury is so constantly employed with so good an effect. In parenchymatous inflammations, especially in *pneumonia* and in *hepatitis*, mercury has been used with asserted advantage by many practitioners, but its value is certainly more questionable than in serous inflammations. Calomel is useful in severe *laryngitis*, and especially in the *pseudo-membranous* variety, when the type is sthenic; and no time should be lost in bringing the system under its influence. The extent of its power to arrest the course of *endocarditis* is certainly an open question; but as it is extremely important, if possible, in this disease, to prevent exudation, and as mercury is the most efficient known agent for effecting this, it should be administered freely and at once. If the disease be of rheumatic origin, the alkalies may be administered conjointly with the mercurial.

In whatever disease a mercurial is administered as an antiphlogistic, it should be given during the stage of exudation, and to facilitate the absorption of the newly-organized lymph after it has ceased to be thrown out. In the majority of cases, mercury given for its constitutional effects should be combined with opium, to prevent its acting on the bowels.

Calomel should not be used in *adynamic inflammations*, or where the exudation is serous rather than fibrinous. In *puerperal peritonitis* it has been strongly advocated by some, and as strongly condemned by others, simply because there are two varieties of the disease, the *sporadic* or *sthenic*, and the *epidemic* or *asthenic;* and in the one both bleeding and calomel are strongly indicated, whilst in the other they are effective only for evil.

Mercury as an Antisyphilitic.—It was formerly believed that syphilis could not be cured without the use of mercury; but latterly there has arisen a school of syphilographers who assert that the drug is not only not necessary, but is at all stages and in all cases of the disease most injurious; that the worst symptoms of the disease are due not to the constitutional affection, but to the remedy given for its relief. The great bulk of the profession occupies a middle ground between these extremes, holding the opinion that whilst mercury is not absolutely essential for the relief of syphilis, it is yet in many cases of the utmost value when judiciously used. The justice of this position cannot, I think, be rightly questioned; the universal verdict in its favor is too fixed and definite; so that the important point now is to determine at what stages, and under what conditions, the remedy is advisable, and what is the best method of its application.

Syphilis is ordinarily, and with sufficient accuracy for practical purposes, divided into three stages, the primary, the secondary, and the tertiary. According to the teachings of the dualists, there are two varieties, or rather species, of venereal ulcer, the hard and the soft chancre, or the true chancre and the chancroid, the infecting and the non-infecting sore. When a venereal ulcer offers the characteristic of the latter of these, mercury should never be exhibited. So long as there is a doubt as to the nature of the primary sore, the remedy should be withheld; but when there is distinct induration, and the inguinal glands begin to be involved, it should be given.

It is proper to state that some high authorities deny the expediency of giving the mercurial until the appearance of distinct secondaries. They affirm that mercury is powerless to prevent the occurrence of these phenomena; that the good which it does is found in its hastening their completion, and consequently that it should be reserved until the second stage of the disorder. I myself believe this is incorrect practice, that minute doses of mercury should be given continuously for many months so soon as undoubted syphilitic symptoms are manifested. The careful experiments of Keys (*Amer. Journ. Med. Sci.*, Jan. 1876) have shown that under these circumstances such small doses act as a tonic, increasing the number of the red blood-discs. Ptyalism is to be avoided unless the symptoms eagerly demand it.

In *tertiary* syphilis, mercury is to be used cautiously, and only in combination with the iodide of potassium. In the *hereditary* syphilis of infants, a decided mercurial impression offers the best chance of relief. Even in the *primary* or *secondary* stages of syphilis mercury should be employed with caution and judgment. In his researches (*loc. cit.*) Wilbouchewitch found that the mercurial when first exhibited increased the number of red blood-corpuscles in syphilitic patients, but after a time appeared to produce anæmia. Whatever preparation be employed, it should be so administered as to exhibit only signs of its constitutional action upon the mouth. It is not necessary to ptyalize the patient severely, or indeed at all, the proper course consisting in the steady maintenance of the slightest possible distinct soreness of the gums. There are various methods by which this may be done. That most frequently employed, because most convenient, is the administration of small doses of calomel or blue pill by the mouth: from one-quarter to one-half a grain of calomel, or twice as much of the blue mass, combined, if necessary, with opium, to prevent its action upon the bowels, may be given three times a day, and increased if required. Instead of the internal use of the mercurial, the system may be brought under its influence by inunctions with the unguentum hydrargyri. When this is done, the skin should be well cleansed and softened by frequent bathing, and then a drachm of the ointment may be rubbed into the inside of the thighs, legs, and the popliteal spaces, in such a way that the application be not made to any spot oftener than every other day.

It is commonly advised in English works to employ the armpits; and, as the skin is there exceedingly thin and the absorbents very numerous, mercury is without doubt more rapidly taken up at that place than at any other part of the body. When, however, mercury is applied to any hairy surface, it very commonly in a short time induces a troublesome eruption, due to inflammation about the hair-follicles. The eruption appears anywhere on the skin if the mercurial ointment be applied too freely; and, in order to avoid this inconvenience, in Germany the following plan is adopted (Dr. H. Zeissl, *Lehrbuch der Syphilis*, Theil ii. p. 349): The patient, having been prepared by thorough warm bathing, and having received about half a drachm of the ointment, is directed to place it in the hollow of the hand and to rub the two hands together until the ointment is equally diffused; then to apply it forcibly and slowly to the part directed until almost all of the salve has disappeared, having been rubbed into the skin. In most cases the mercurial is applied daily; but in very susceptible persons only every third day. A regular order is maintained in the application, as follows: *First day*, inner side of both upper arms; *second day*, inner side of both thighs; *third day*, inner side of both fore-arms; *fourth day*, inner side of both legs; *fifth day*, upon both groins; *sixth day*, upon the back; *seventh day*, recommence the series.

The advantage claimed for inunction is that the digestion is less apt to be disturbed than when the drug is exhibited by the mouth; the disadvantages are the greater or less publicity which it entails, the trouble which it involves, and its apparent dirtiness. In private practice it is rarely used except in the case of infants, when the mercurial ointment is rubbed into the abdomen and armpits, or often simply smeared upon the flannel roller or binder which usually envelops the body. The mercurialization of the nurse, with the object of affecting the child, is unjustifiable, unless the nurse and the nursling are alike diseased: indeed, to allow a syphilitic child to feed at the breast of a healthy woman is extremely reprehensible.

Mercury is sometimes administered in secondary syphilis in the form of fumigations. The patient is placed upon a chair, and surrounded by a large blanket, or, better, india-rubber cloth, so arranged as to fit tightly around his neck above, and below to encompass the chair. The mercurial preparation is placed upon a metal plate, heated by a spirit-lamp, beneath the chair, and the fumes are allowed to fill the space around the patient inside of the blanket.

The heat produced generally causes the patient to sweat profusely, and in from fifteen minutes to half an hour the lamp should be withdrawn, and the patient allowed to cool off, and after a time be put to bed and wrapped up in blankets, with the deposit of mercury still adhering to his skin. The fumigation may be practiced every other night, or at longer intervals, and is believed by some to be especially useful in cases of secondary skin-eruptions. Calomel, black oxide, and cinnabar are the preparations generally used. When the last is employed, care must be exercised that the patient do not breathe the fumes.

In advanced secondaries, the iodides of mercury, given by the mouth, are to be preferred. They should never be pushed to the point of producing salivation.

In tertiary syphilis, mercury should rarely, if ever, be exhibited by itself, but the combination of the corrosive sublimate and the iodide is often more efficient than the latter drug alone. In most cases not more than one-twelfth of a grain of the bichloride should be given, three times a day.*

ADMINISTRATION.—The following preparations contain metallic mercury:

Unguentum Hydrargyri, U. S.—*Blue*, or *Mercurial*, *Ointment* is made by triturating mercury with suet and lard, until the metal is extinguished,—*i.e.*, until a portion of the mass rubbed upon a piece of paper exhibits no globules under a magnifying power of four diameters. Mercurial ointment is soft, of a bluish color, becoming darker by age, and contains half its weight of mercury. When frequently rubbed upon the same part, it not rarely produces a disagreeable eruption. It is used to make a constitutional impression, and also locally as a resolvent in cases of enlarged *indurated glands*. The *oleate of mercury* (*Hydrargyri Oleatum*—1 to 10, U. S.) appears to be a more elegant preparation than blue ointment, and equally efficient.

Emplastrum Hydrargyri, U. S.—*Mercurial Plaster* contains mercury, olive oil, resin, and lead plaster, and is used as a resolvent in *indurated glands*, enlarged *chronically inflamed joints*, etc.

Massa Hydrargyri, U. S.—*Pills of Mercury*—*Blue Mass* is made by extinguishing mercury with honey and other inert substances. It contains one-third its weight of the metal, and is used for the same purpose as calomel, but is milder. Dose: purgative, grains 5 to 10; alterative, grains 1 to 3. "*Blue Pills*" usually contain each three or five grains of the mass.

Hydrargyrum cum Creta, U. S.—*Mercury with Chalk*—*Gray Powder* is made with chalk. It is a smooth, grayish powder, and is similar in its medical properties and strength to blue mass.

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* The hypodermic use of mercury does not seem to me justifiable. As to relations of sublimate to albumen and albuminous compounds for hypodermic use, consult *Arch. Exp. Path. et Pharm.*, iii., 1875; *Wiener Med. Woch.*, xxvi. 11, 1876. M. M. Martineau claims that ammoniacal mercurial peptones may be used hypodermically in syphilis with great advantage. The formula may be found in *Lond. Med. Record*, 1882, p. 47.

HYDRARGYRI CHLORIDUM MITE—MILD CHLORIDE OF MERCURY. U.S.

Calomel is made by boiling mercury and sulphuric acid together in such proportions as to form a bisulphate of the deutoxide of mercury, reducing this to the simple sulphate of the protoxide of mercury by triturating it with more of the metal and subliming with the chloride of sodium. The sublimate is to be well washed with water, to remove any of the bichloride that shall have been formed owing to the imperfect reduction of the bisulphate to the sulphate. When the washings are no longer affected by the addition of ammonia, it may be known that the drug is free from the soluble corrosive sublimate. Calomel is sometimes manufactured by precipitating corrosive sublimate by sulphurous acid; but this method is not officinal, and is subject to serious disadvantages.

Physiological Action.—Owing to the great insolubility of calomel, a good deal of discussion has occurred as to the way by which it finds entrance into the system. The theory of Mialhe (*Chimie appliquée*), a modification of one originally advanced by Snow (*Lancet*, 1840), has been pretty widely accepted, though with some hesitation, but is, I think, untrue. According to the chemist named, the calomel is converted by the chlorides of the stomach into corrosive sublimate, and as such is absorbed. The action of calomel upon man is so different from that of corrosive sublimate as to render this theory exceedingly improbable, and, at temperatures even higher than that of the stomach, Mialhe was never able to obtain the formation of more than a sixteenth of a grain of the sublimate by the gastric juices. Further, Bucheim, Oetingen, and Winkler (quoted by Prof. Stillé, *Therapeutics*, 2d ed., p. 655) affirm that this conversion does not occur at all at the temperature of the body. Jeannel (*Schmidt's Jahrbücher*, Bd. cxliii. p. 9; from *Journ. de Bordeaux*, 4e sér., t. ii. p. 67, 1869) has confirmed this, and has suggested what seems to be the way in which calomel is absorbed. He finds that when the protochloride of mercury is placed in a solution of an alkaline carbonate it is decomposed and the gray oxide precipitated. A small portion. however, of the latter is held in solution, as much as 0.02 part in 50 parts of water (by weight); and if a fatty oil be mixed with the alkaline solution a very large part of the mercury is dissolved. From these facts it would seem to follow that the calomel entering the stomach escapes unchanged into the alimentary canal, and is there decomposed by the alkaline juices and dissolved by the fatty matters always present. The physiological evidence appears to confirm this, for calomel, being absorbed in this way, ought to resemble blue mass rather than corrosive sublimate in its action,—which it does.

The varying constitution of the alimentary juices and the complex chemical relations of calomel would indicate that its solution in the alimentary canal is accomplished in more ways than one,—an indication which is confirmed by the varying results following the ingestion of the drug. It is probable that at times, when the stomach contains more than usual of chlorides and of hydrochloric acid, a very slight portion of the calomel is converted into corrosive sublimate, and that when there is an excess of sulphuretted hydrogen in the alimentary canal a soluble sulphide may be formed. Calomel has been used subcutaneously (Dr. F. Zambon, *Gaz. Med. Ital. Prov. Venete; The Doctor*, 1871), with asserted good results, in syphilis;* and, according to Bellini, its solution is due to the presence of alkaline chlorides in the system. He states that very severe constitutional and local symptoms may follow the hypodermic injection of calomel in persons taking the alkaline iodides, bromides, or sulphates. The influence of calomel upon the system has been sufficiently discussed. It remains only to state that its freedom from all irritant properties is shown when taken internally or when used externally. Probably no single dose of it is capable, in the average man, of acting as a violent poison, since it is stated that in the Western United States it is very frequently taken in teaspoonful doses, that sixteen grains of it will act as vigorously as an ounce, and that a pound of it has been given in a case of cholera without visible effect.† It seems to me most probable that the absence of serious results from these heroic amounts is due to the alimentary canal being unable to dissolve—*i.e.*, to absorb—the calomel. F. D. Lente has claimed that given in this way the drug acts as a sedative and does not produce mercurialization, and Mrs. Putnam-Jacobi believes such doses to be valuable in diseases where there is "sudden over-distention and paralytic congestion of extensive regions of small blood-vessels." (See *New York Med. Journ.*, xi., 1870; xxix., xxx., 1879.)

ADMINISTRATION.—When it is desired to produce constitutional mercurialization, the dose of calomel is a half to one grain; as a purgative, from six to ten grains are administered, and followed in six hours by Seidlitz powder, or other saline, if required. Minute doses (one-sixth of a grain) of calomel given every hour afford a very good method of impressing the system rapidly. When it is desired to get its constitutional influence, it is generally necessary to conjoin opium with it, to prevent purging.

HYDRARGYRI CHLORIDUM CORROSIVUM—CORROSIVE CHLORIDE OF MERCURY. U.S.

Bichloride of Mercury, or *Corrosive Sublimate*, is made by subliming the bisulphate of mercury with common salt. It occurs in the form of colorless crystals, or of white, semi-transparent, crystalline masses, of an acrid, metallic, styptic, and very persistent taste, soluble in sixteen parts of cold and in three of boiling water. It is at once distinguished from the other mercurial preparations by its color, taste, and solubility, and by its forming a yellow precipitate with lime-water.

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* See also Prof. R. Bellini, *Lo Sperimentale*, June, 1873; *London Medical Record*, 1873; Kölliker, *Centralb. für Chir.*, 1877, 97.

† Prof. George B. Wood's *Therapeutics*, vol. ii. p. 565.

Physiological Action.—Corrosive sublimate is a violent irritant, and in concentrated form caustic. When given in small, repeated doses, although capable of inducing salivation, it is less apt to do so than is calomel or blue pill. In overdoses it produces symptoms of irritant poisoning of a severity proportionate to the dose. If the latter be small, the manifestations may be only some nausea, slight burning in the stomach, colicky pains in the abdomen, and diarrhœa. After large doses these symptoms are intensified. The subject first experiences a peculiar metallic, coppery taste at or shortly after swallowing the poison. If the solution be concentrated, deglutition is interfered with by a spasm of the muscles of the throat and larynx, causing a feeling of suffocation, and sometimes even the rejection of the draught. Then burning pains are experienced in the œsophagus and stomach, followed by violent vomiting, at first mucous, then bilious, and finally bloody, and by severe abdominal pain and tenderness, with profuse purging, at first serous in character, but afterwards affording only small, mucous, bloody stools, which are often voided with much straining. The breath generally becomes fetid and offensive in a very short time. In the course of two or three hours, very rarely in less than an hour, collapse occurs, with small, frequent, irregular pulse, pinched, anxious face, cold extremities, and finally death, preceded, it may be, by fainting, convulsions, and coma. The urine is very much lessened in quantity, is sometimes albuminous, or even bloody, and not rarely is suppressed. If the patient survive several days, a petechial eruption may appear, and salivation sometimes, but not always, occurs. In some cases, after the collapse there is an attempt at a febrile reaction, which soon, however, gives place to a second and fatal prostration. When recovery occurs after severe poisoning, the convalescence is slow and protracted.

In regard to chronic poisoning with corrosive sublimate, sufficient has been said under the general heading, except that colicky pains and abdominal disturbance are more apt to occur with it than with the less irritating preparations. MM. Arnozan claim that chronic catarrh of the excretory ducts of the pancreas is a pronounced lesion in chronic poisoning of animals (*Journ. de Bordeaux*, Dec. 1883). It should be looked for in man, and its presence might be of medico-legal value.

Severe purging, and even fatal poisoning, may result from a single external application of this preparation of mercury;* and in animals killed by hypodermic injections of it (see experiments of Dr. J. Rosenbach,

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* See case reported by Dr. Meeres, *Lancet*, Sept. 16, 1871, in which a solution (gr. ii to f ʒi) was applied with a camel's-hair brush to the head of a child nine years old, for the cure of tinea tonsurans. The symptoms were diarrhœa, profuse salivation, and great prostration, ending in death. Washing out vagina and uterus with a very weak solution of corrosive sublimate (one in two thousand) has caused severe poisoning (*Centralb. f. Gynaekol.*, 1884, No. 13, No. 17).

Schmidt's Jahrbücher, Bd. cxliii. p. 9) diarrhœa and other indications of gastro-intestinal irritation are prominent symptoms,—facts which indicate that the bichloride is eliminated unchanged from the alimentary canal.

HYDRARGYRI IODIDUM VIRIDE—GREEN IODIDE OF MERCURY. U.S.—This *Protiodide of Mercury* is made by the direct action of iodine upon the metal. It is a greenish-yellow, odorless, and tasteless powder, insoluble in water, ether, and alcohol. Compared with the biniodide or the bichloride, it is a mild preparation, and has been used to produce constitutional impression in *syphilis*, especially when of long standing. The iodide of potassium converts it into the biniodide and metallic mercury (U. S. Dispensatory), and should, therefore, never be given in combination with it. The alterative dose is one-fourth of a grain three times a day, increased to a grain if necessary.

HYDRARGYRI IODIDUM RUBRUM—RED IODIDE OF MERCURY.—The *Biniodide of Mercury* is made by precipitating the bichloride of the metal with iodide of potassium. It is a scarlet-red powder, insoluble in water but sparingly soluble in alcohol. It is a powerful local irritant, producing, when taken in overdoses, symptoms and results very similar to those caused by corrosive sublimate. It is used a good deal in *tertiary syphilis* and in *syphilitic rheumatism;* also to some extent as a local application in *lupus* (see *Annuaire de Thérap.*, 1852). It is much more active than the protiodide, and should be used as cautiously and in the same doses as corrosive sublimate.

The U. S. Pharmacopœia also recognizes the following preparations of mercury:

The deutoxide occurs in two forms, the *Yellow* and the *Red Oxide* (HYDRARGYRI OXIDUM FLAVUM, HYDRARGYRI OXIDUM RUBRUM). Both are used upon *ulcers*, *chancres*, etc., solely for their local effects, and are stimulant and alterative when diluted, mildly escharotic when in powder. From Hydrargyri Oxidum Flavum is made the *oleate* (*Oleatum Hydrargyri*—1 to 10, U.S.). The *red Precipitate Ointment* (*Unguentum Hydrargyri Oxidi Rubri*, 1 to 10, U. S.), and the *ointment of the yellow oxide* (*Unguentum Hydrargyri Oxidi Flavi*, 1 to 10, U. S.), very generally require dilution with lard, and are much used in chronic *skin-affections*, in obstinate *conjunctivitis*, in *psorophthalmia*, etc.

The *Red* or *Bi-sulphuret* (HYDRARGYRI SULPHIDUM RUBRUM, U. S.), formerly used a good deal in fumigations, is now rarely employed. *Turpeth Mineral*, or *Yellow Sulphate of Mercury* (HYDRARGYRI SUBSULPHAS FLAVUS, U. S.), a lemon-yellow powder, sparingly soluble in water, is a basic sesquisulphate of the deutoxide of mercury, prepared by throwing the bisulphate into water, which causes it to break up into a supersulphate, which remains in solution, and the salt in question, which precipitates. Turpeth mineral has been used as a harsh emetic, and also as an alterative, but is now rarely employed. In *croup*, in emetic doses it is still very highly esteemed by some practitioners, and has been inordinately praised by Dr. Fordyce Barker. It is, however, a very dangerous remedy, since, if it fail to vomit, it may cause a fatal gastro-enteritis, especially in the young child. Two cases of such character are recorded by Dr. A. McPhedran (*Med. News*, xliii. 682). The dose as an alterative is from a quarter to half a grain; as an emetic, for a child two years old, two grains repeated in fifteen minutes, if it has not operated. Forty grains of it (*Guy's Hospital Reports*, vol. x., 3d series) have caused death in the adult; profuse salivation came on in six hours.

White Precipitate, or *Ammoniated Mercury* (HYDRARGYRUM AMMONIATUM, U. S.), is a white complex powder, made by precipitating the bichloride with water of ammonia. It is used in the form of ointment (*Unguentum Hydrargyri Ammoniati*—1 to 10, U. S.) as a local application in various skin-affections.

Black Wash and *Yellow Wash*, two non-officinal but favorite preparations, are respectively made by the addition of a drachm of calomel to a pint of lime-water, and of half a drachm of corrosive sublimate to a pint of lime-water. They depend for their virtues upon the black and yellow oxides of mercury, and are used exclusively as local applications to *chancres* and other *syphilitic ulcers*. The yellow wash is much the more stimulating of the two.

IODUM—IODINE. U.S.

Iodine is a soft, friable, opaque substance, occurring in crystalline scales with a semi-metallic lustre and of a bluish-black color. Its odor resembles that of chlorine; its taste is hot and acrid. It is somewhat volatile at ordinary temperatures, but when heated to 225° F. melts and emits the beautiful purple or violet vapor to which it owes its name. It is freely soluble in glycerine, alcohol, and ether, but requires seven thousand times its weight of water to dissolve it. With starch it strikes a deep-blue color, and this test is so delicate that it will indicate the presence of iodine in four hundred and fifty thousand times its weight of water. In testing animal liquids, such as urine, for iodine, a small quantity of nitric acid should be added to insure its being free in the liquid.

PHYSIOLOGICAL ACTION.—Iodine, when applied to any part of the body, acts as a very powerful irritant, or, if in highly concentrated form, as a mild caustic. The tincture stains the skin yellow, and causes, if applied with sufficient freedom, smarting, some erythematous inflammation, and finally desquamation. Its repeated application blisters and destroys the cuticle. Upon mucous membranes its action is more intense than upon the skin.

When taken internally, a single moderate dose of iodine causes merely some gastric uneasiness and a disagreeable metallic taste in the mouth; when larger amounts are ingested, the gastric uneasiness may be intensified into violent vomiting, with increased salivary flow, abdominal pains, and even purging. In sufficient quantity it is a poison; although very few deaths have been recorded as caused by it. The usual symptoms, when toxic doses of it have been taken into the stomach, are vomiting, purging, severe abdominal pain, headache, giddiness, sometimes violent excitement and convulsions, ending in faintness, pallor, and collapse. Dr. E. Rose (*Nothnagel's Arzneimittellehre*, Berlin, 1870, 252) has reported a case in which death resulted from a large injection into an ovarian cyst. Very soon after it was given, there ensued severe thirst, with great dryness of the throat and mouth, and then painless vomiting of watery matters containing iodine. The whole surface became very pale, the extremities cyanosed; the radial pulse very frequent, but so small that it could not be counted; the urine very scanty, dark brown, and rich in iodine. After a time, reaction occurred. For three days the vomiting persisted, the pulse was very frequent, full and hard, and the cheek put on the glow of high fever, but the temperature did not rise above 37.18° C. On the fourth day, exanthematous blotches, not disappearing on pressure, appeared on the skin and in the mouth; the sputa became bloody; and menstruation occurred, two and a half weeks too soon. The urine remained scanty, and on the eighth day, when all other symptoms save swelling of the parotids had disappeared, still contained iodine, and was albuminous. On the tenth day, in the midst of apparent convalescence, the patient died suddenly.

In the experiments of Jörg and his pupils, doses of iodine of a grain to a grain and a half gave rise to colicky pains, increased appetite, watery stools, an increased secretion of urine, malaise, and some headache. When the dose was augmented to two grains, a diffused sense of heat and sexual excitement were superadded. Other observers have noted this abnormal sexual excitement, and some have stated that at times it precedes atrophy of the mammæ or of the testicles. Prof. Stillé affirms that the menstrual flow may become excessive, or that during pregnancy abortion may be caused. Very large quantities of iodine are asserted to have been taken without serious results. Julia de Fontenelle (quoted by Stillé, *Therapeutics*, ii. 731) tells of a man who took two and a half drachms of iodine without experiencing any remarkable effects; and Magendie relates the case of a child four years old who swallowed ten grains without serious consequences.[*]

In the experiments of A. Höyges and Prof. Binz (*Arch. Exp. Path. und Therap.*, x. 229; xiii. 114), preparations of iodine, iodide of potassium, and iodoform in fatal doses produced in the lower animals wide-spread fatty degenerations.

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[*] For an elaborate, careful study of the action of large toxic doses of iodine upon the lower animals, see *Hoffmann und Schwalbe's Jahrsbericht*, 1879, 199.

If full doses of iodine be exhibited continuously for a length of time, a train of phenomena result, known as *Iodism*. In regard to these there has been a good deal of difference of opinion and statement, a difference which seems explainable only upon the supposition that different individuals are differently affected by the drug. Rilliet (Trousseau's report on his memoir, *Bull. de l'Acad. Roy.*, xxv.), who has had wide opportunities and has apparently studied the subject very closely, makes three forms of iodic intoxication: first, that in which the symptoms are those of gastric irritation; second, that characterized by nervous troubles, neuralgia, ringing in the ears, convulsive movements, disturbed intellection, with coryza, ophthalmia, salivation, vomiting, diarrhœa, polyuria, and cutaneous eruptions, and in some cases atrophy of the mammæ in the female and of the testicles in the male;* third, iodic cachexia, caused either by iodine or iodide of potassium continuously used for many months. It is said to be most easily induced in goitrous persons, and is characterized by rapid emaciation, commencing mostly in the face, and severe nervous palpitations of the heart, with excessive appetite, which sometimes precedes and sometimes follows the loss of flesh. So long as the drug continues to be taken, these symptoms continue to progress, and after a time hysteria or hypochondriasis, with insomnia, manifests itself. The goitre, the mammæ, and the testicles waste away together; but if the medicine be suspended and health gradually return, whilst the abnormal growth reappears, the sexual glands remain wasted.

The second form of iodism of Rilliet, in which the nervous symptoms are prominent, has been spoken of by other authorities; and Brodie has especially noted disturbances of vision, and paralysis.

Most authorities affirm that iodine and iodide of potassium produce similar symptoms. Prof. Sée (*London Med. Record*, i. 777) indeed asserts that iodine exists in the blood only in the form of an alkaline iodide, whilst Dr. H. Kämmerer (*Virchow's Archiv*, lix. 467; lx. 527) and Prof. Binz believe that the iodides are decomposed in the tissues and act by the liberation of the iodine.† I do not think, however, that these views can be accepted as completely established, and the general professional belief is that the therapeutic value, and consequently the physiological action, of iodine and iodide of potassium are different. Iodine is universally preferred in scrofulosis, the iodide in rheumatism. I have given the salt in enormous doses, and have seen nervous symptoms in only a single case,—a man who received for a long time two hundred and seventy grains a day, and who was intensely sleepy and stupid, presenting symptoms exactly similar to those of bromism, including an eruption of acne.

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* For a case of wasting of testicles, see *Phila. Med. Times*, iv. p. 661.

† Consult also Prof. Bucheim (*Arch. Exper. Pathol. und Therap.*, Bd. iii.). Dr. Dubujadoux (*Gaz. Hebd.*, 1883, xx. 24) found that iodine injected into guinea-pigs suffering from malignant pustule, had no influence upon the disease, even if the injections be repeated until they killed the animal, and that the blood also is as poisonous as ever to other guinea-pigs. This led him to believe that the iodine exists in the blood in a new compound which is not antiseptic. He believes this compound to be albuminous, because he has found iodine mixed with milk or albuminous solutions soon disappears, so that it cannot be recognized by the starch test, and that shortly after this disappearance putrefaction sets in.

Of the physiological action of iodine we know little more than that it modifies nutrition. Locally the drug is an irritant, and sometimes gastric symptoms are produced by it from this cause. The general erethism which it induces is believed by Prof. Sée to be produced by a direct excitement of the circulation, and even the nervous symptoms are attributed to the same cause,—all of which is very improbable. Iodine is certainly absorbed and is eliminated chiefly by the kidneys, but probably to a greater or less extent by all the mucous membranes; and Dr. R. W. Taylor (*American Journal of Syphilography and Dermatology*, April, 1873) believes that he obtained in a case evidences of the free escape of the iodine through the skin. Prof. Sée asserts (*London Med. Record*, i. 757) that the elimination takes place slowly and intermittently, so that the drug when given continuously accumulates in the system. He further states that it can be found in the saliva after it has disappeared from the urine. The iodine seems to be eliminated partly as an alkaline iodide and partly in organic combination (E. Harnack, *Berlin. Klin. Wochensch.*, 1882, No. 20).

During its passage through the kidneys iodine undoubtedly exerts an influence upon those organs, as is shown by its producing albuminuria at times. It is indeed asserted that it occasionally causes a true tubular nephritis. The evidence as to its effect upon the solids of the urine is both contradictory and insufficient. M. Rabuteau[*] dieted himself for five days, measured the quantity of urea daily eliminated, took iodine on the fifth day, and found a decided decrease in the excretion of urea. It is plain that this experimentation was too slight to be of much value, and Dr. Hermann von Boeck (*Zeitschrift für Biologie*, iii. 393, 1869; *Schmidt's Jahrbücher*, Bd. cxlv. p. 142) found that the ingestion of iodine does not increase notably the elimination by the kidneys or bowels. On the other hand, M. Bouchard (quoted by Sée) declares on his personal experience that iodine does increase the daily elimination of urea, especially in diabetic patients. Dr. C. Handfield Jones (*Beale's Archives*, i.) analyzed the urine of six patients taking large doses of iodide of potassium, with the following results: first, water increased in three cases very much, in one slightly so, in two diminished; second, acidity increased in three and diminished in two; third, urea increased in three and diminished in three; fourth, phosphoric acid and sulphuric acid increased in four and diminished in two; fifth, chlorine increased very greatly in two cases, moderately in one, and decreased in two; sixth, uric acid increased very greatly in two cases and diminished in four.

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[*] Quoted by Sée.

THERAPEUTICS.—As an alterative, iodine is of especial value in *chronic scrofula*. In those cases in which there is indolent enlargement of the lymphatics, which exhibit no tendency, or but little tendency, to suppurate, it is of especial value. Except in very acute cases, however, it should always be tried, even when the glands do tend towards suppuration, especially as it exerts a very beneficial influence upon the ulcers left after suppuration. In other forms of scrofulous disease, in *chronic enlargements* of the *joints*, and *bone-affections* of such nature, iodine is often of great service. As scrofulosis is generally, if not always, associated with lowered nutrition and with anæmia, cod-liver oil and iron in some form should usually be administered as adjuvants. At the same time that the drug is exhibited internally in these cases, its ointment should be freely applied to the enlarged and indurated glands. Experience has demonstrated the value of iodine in *goitre*, whether of the ordinary variety or of that known as *exophthalmic goitre* or *Graves's disease*. All tumors of the thyroid body are not goitre, however; cystic degeneration of it is very common, and is in no wise benefited by iodine. It is in simple hypertrophy of the gland that iodine used internally and applied externally over the tumor is so beneficial. During the acute stage of enlargement the use of leeches is often of great benefit, and whenever much tenderness exists should precede the exhibition of the drug. In *phthisis*, iodine sometimes does good, but only in the most chronic cases; and inhalations of its vapors, as have been recommended by Piorry, can only be of service by stimulating the bronchial mucous membrane and the surfaces of cavities. When softening is progressing and the lung breaking down, iodine sometimes appears to hasten the process.

Local Application.—As a simple counter-irritant, iodine is very frequently employed when it is desired to maintain a mild, persistent influence, as in *chronic rheumatic affections* and sometimes in *phthisis*. For this purpose the tincture is generally preferred, and it should be applied freely once or twice a day, or every other day, according to the susceptibility of the patient's skin. In various affections of the skin, iodine has been employed with asserted advantage. In *erysipelas* of the skin, very beneficial results have been ascribed to its local use, and, I think, with justice; but great care is necessary lest it be applied too strong. I have seen very serious results from the destruction by it of the skin in this affection. If the full strength of the tincture be used, it should be applied at first very lightly, and not more than once in the twenty-four hours. In *psoriasis*, in *acne*, in *parasitic skin-diseases*, it has been used, but holds only a second rank among remedies. In a similar manner it is employed in various chronic diseases of the mucous membranes, such as *ozæna*, *leucorrhœa*, *chronic cystitis*, *chronic dysentery*, and scrofulous *ophthalmia*,—whenever, in a word, an alterative, stimulant action is desired. In cases of *retraction* of the *gums*, with consequent loosening of the teeth, Prof. Stillé recommends the application, with a camel's-hair brush, after each meal, of a watery solution (gr. i to f℥i) of iodine, the mouth being immediately afterwards washed. The most important external use of iodine is as a resolvent in cases of indolent *glandular* hypertrophic enlargement, and where there are large watery exudations, as in some forms of *chronic pleurisy* and of *diseased joints.*

Iodine has been very largely employed by injection into serous cysts, as in *hydrocele,* for the purpose of exciting inflammation and causing obliteration of their cavity; but this use of it is purely surgical, and the reader is referred to treatises upon such subjects. In chronic *empyema,* the injection of iodine after free exit has been given to the pus is often of the greatest service. The solution in the beginning should be very weak, containing not more than six grains each of iodine and of iodide of potassium in a pint of water; with this the pleura should be daily washed out, the strength of the solution being gradually increased.

ADMINISTRATION.—Iodine is never administered in solid form; nor should the tincture be given internally, because the iodine is precipitated by the watery juices of the stomach. Taking advantage of the solubility of iodine in a watery solution of iodide of potassium, the framers of the Pharmacopœia have directed the following preparations, which may be used internally; they should always be given well diluted, after meals; any of them may be used hypodermically, as suggested by Prof. Da Costa (*Amer. Journ. Med. Sci.,* Jan. 1875), in glandular enlargements:

Liquor Iodi Compositus—Compound Solution of Iodine—Lugol's Solution (Iodine, 1 part; Iodide of Potassium, 2 parts; Water, 17 parts),—dose, gtt. v to xv.

For external use, a *tincture* (*Tinctura Iodi,* 1 to 12.5), and an *ointment* (*Unguentum Iodi:* Iodine, 4 parts; Iodide of Potassium, 1 part; to 100).

POTASSII IODIDUM—IODIDE OF POTASSIUM. U.S.

This salt occurs in white or colorless, generally cubic, crystals, soluble in two-thirds of their weight of water and in from six to eight parts of rectified spirits. If to its solution starch be added, no blue color should arise, but on the passage of chlorine the characteristic iodine reaction should take place, owing to the liberation of the metalloid by the gas; or if sulphuric acid be added, a purple tint gradually appears, and deepens into blue: a spontaneous blue color betrays the presence of the iodate of potassium, a harmful adulteration. At a dull red heat iodide of potassium fuses into a crystalline mass; by a bright heat it is decomposed.

PHYSIOLOGICAL ACTION.—Iodide of potassium influences nutrition in a manner similar to iodine: indeed, most authorities teach that their action is identical; yet in therapeutics they find a different range of employment, and, I believe, act differently. Dr. I. Wallace (*Liverpool Med. and Surg. Rep.,* 1871) has found that the iodide lessens the elimination of lime salts through the kidneys, but his analyses were not sufficiently repeated to prove that this is a constant effect.*

THERAPEUTICS.—In certain forms of *rheumatism*, iodide of potassium is of the utmost value. In the early, active stages of *inflammatory rheumatism*, it is much less efficient than the alkalies; but when all the good that can be has been obtained from these, and when the joint symptoms persist in a subacute form, the iodide comes very well into play. In *subacute* or *muscular rheumatism*, the iodide is the most efficient remedy. Often when the symptoms are very acute it may be advantageously combined with the alkalies, and in lingering cases, especially where there is reason to suspect a gouty taint, with colchicum. In *sciatica*, in *lumbago*, in *rheumatic neuralgia* following exposure to cold or wet, as in all other forms of subacute rheumatism, very much is to be hoped for from its use. In *gout*, it is of less service than in rheumatism, but in the chronic form of the disease, and in the irregular, inherited gout which so frequently appears as neuralgia or other anomalous affection, it adds to the efficiency of small continuous doses of colchicum. In *rheumatic gout*, or *rheumatoid arthritis*, it should be tried; although little is to be hoped for from its use. There is a good deal of clinical testimony as to the value of iodide of potassium given continuously between the paroxysms of *asthma*. This disorder appears at times to bear a close relation to irregular gout or rheumatism, and it is probably under these circumstances that the remedy is efficient. In *tertiary syphilis*, including in the term all cases of syphilitic bone, visceral, or nervous disease, the remedy is really of inestimable value. It must be given freely, and, when there is no cachexia, may be advantageously combined with the bichloride of mercury. It is scarcely in place here to enumerate all the forms which tertiary syphilis may assume; but the iodide is useful wherever the dyscrasia has existed for a length of time.

The iodide of potassium appears to have the power of promoting absorption of serous fluids, and certainly is of value in *chronic pleuritis* with effusion, in *chronic pericarditis*, and even in *chronic hydrocephalus*.

In aortic *aneurism* large doses of iodide of potassium with continuous rest in the horizontal position have been used by Dr. Balfour (*Edinburgh Med. Journ.*, xiii., xiv., xv., xvi.; *British Med. Journ.*, 1874, i. 112) with results that warrant a further trial. Dr. T. S. Sharpe claimed success from its employment in chronic Bright's disease (*Amer. Journ. Med. Sci.*, Jan. 1876).

In various chronic *metallic poisonings*, the iodide of potassium is of great service. With both lead and mercury it forms double salts, which are soluble, and there is very good reason for believing that the formation of these salts takes place in the economy, and that the metal which has been lying in an insoluble condition in the various tissues is taken up and excreted. Severe salivation and ulcerative stomatitis have sometimes resulted from the use of the potassium salt in those who had previously taken large quantities of mercury;* and in Melsen's experiments, dogs to which insoluble preparations of mercury had previously been given without the induction of severe symptoms afterwards died under the action of the iodide, the mercury also having appeared in their urine. The experiments of Mayençon and Bergeret, quoted in the article on Mercury, afford striking confirmation of these facts, and seem to render the evidence irresistible that the iodide does cause the elimination of mercury. In regard to lead, the researches of Drs. Parkes, Goolden, Swift, Melherbe, and Sieveking † have shown that very frequently, in cases of chronic lead-poisoning, the exhibition of iodide of potassium causes the appearance of lead in the urine. This chemical evidence is abundantly corroborated by clinical experience, so that in all cases of chronic metallic poisoning, especially by lead and mercury, the persistent use of the iodide of potassium should be tried.

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* For a research upon the physiological action of large amounts of iodide of potassium injected into the blood, see *Arbeiten aus dem Pharmak. Laborator. zu Moskau*, i. 125. As it does not seem to throw much light upon the therapeutic use of the drug, it is not here analyzed.

ADMINISTRATION.—The ordinary dose is ten grains three times a day; but much larger quantities may often be given with impunity, and, in internal syphilitic affections, may be necessary. In the latter class of diseases, the best plan is to begin with twenty grains three times a day, and rapidly to increase the amount until drachm doses are reached, or frontal pain or other symptom of iodism produced. The best substance for disguising the very disagreeable taste of the drug is the compound syrup of sarsaparilla. *Unguentum Potassii Iodidi*, U. S., contains about one-eighth its weight of the iodide.

LIQUOR ARSENII ET HYDRARGYRI IODIDI, U. S.—*Solution of the Iodides of Arsenic and Mercury* contains one per cent. each of the iodide of arsenic and the red iodide of mercury. It was originally suggested by a surgeon of Dublin, by whose name it is very generally known. *Donovan's Solution* is a powerful alterative, used chiefly in very obstinate chronic scaly *skin-diseases* when the local action is of a very low grade, and in *chronic rheumatism*. It is an exceedingly active preparation, very capable of acting as a corrosive poison, and when administered a little too freely is said sometimes to cause salivation. When applied locally, it acts as a violent irritant. The dose of it is from three to ten drops, well diluted.

IODOFORMUM—IODOFORM. U. S.

This substance was discovered by Sérullas in 1822, and was introduced as a remedy by Dr. Glover in 1837, but did not become officinal until the last revision of the U. S. Pharmacopœia. It occurs as small, pearly-yellow

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[*] See Dr. Budd, *British and For. Medico-Chir. Rev.*, xi. 202, for a striking case.

[†] See Stillé's *Therapeutics*, vol. ii. p. 735, Blanchard and Lea, 1864.

crystals, having a strong, persistent, saffron-like odor, insoluble in water, but readily soluble in alcohol and ether.

PHYSIOLOGICAL ACTION.—According to M. Maître, when taken by man in doses of five or six grains iodoform causes no notable symptoms, but two hours after the drug has been ingested, iodine can be found in the urine. The extensive surgical use of iodoform has led to a number of poisonings by it. The symptoms are variously described, and it is almost certain that in some cases they have been due to the wound and not to the dressing. They may be preceded by general malaise for a day, and then suddenly burst forth (Case, *Deutsch. Med. Wochensch.*, ix. 443). In the most characteristic and severe class of cases the phenomena resemble somewhat those of meningitis, and may be somnolence, deepening into stupor, with contracted motionless pupils, or restlessness, ending in active delirium, in either case the temperature being normal and the pulse exceedingly rapid. A peculiarity of these cases seems to be that death usually follows, although the symptoms have developed abruptly and the dressings have been removed at once. Dr. Schede, of Hamburg, describes six classes of cases, his sixth form being that just spoken of. 1. High fever, without other phenomena. 2. Fever, with mild gastro-intestinal irritation, depression of spirits, and rapid pulse; recovery almost invariable. 3. Very rapid, soft pulse, 150–180, no fever; great danger. 4. Very rapid pulse, with high fever; death almost invariable. 5. After severe operations, rapid collapse and death. A form of poisoning with melancholia, dilated pupils, and hallucinations is also described. A roseola-like dark-red eruption has been noted in some cases of poisoning.

The action of iodoform upon the lower animals has been investigated by a number of observers, but to complete our knowledge further researches are necessary. The symptoms in the frog are said to be muscular relaxation with sometimes, at a later stage, convulsive movements. In the higher animals large but non-toxic doses produce symptoms of intoxication, tottering, weakness, and loss of appetite, but no vomiting; fatal doses cause anæsthesia, narcosis, convulsions, with violent opisthotonos, hurried or irregular breathing, slow, feeble pulse, and finally death. A. Höyges found that in dogs and cats toxic doses caused deep sleep without loss of reflex activity; but that in rabbits no sleep resulted (*Arch. Exp. Path. und Therap.*, Bd. x. 405). Very frequently after these large doses, especially when they are repeated, there is great gastro-intestinal disturbance, as is shown by vomiting, diarrhœa, and dysentery, with bloody discharges. The action of the drug upon the circulation has been especially studied by M. Rummo (*Arch. de Physiolog. Norm. et Pathol.*, 1883, 144). He finds in the frog the rate of the cardiac pulsations is lessened, and for a time the energy of the ventricular systole is increased, but afterwards the pulsations become feeble, and finally the heart is arrested in diastole; the contractions cannot be re-established by the use of atropia. In the mammal, the rate of the pulse is decreased, and after small doses, the arterial pressure at first increased. By large doses the pressure is much diminished. Section of the pneumogastrics does not affect the cardiac action of the drug. M. Rummo finds that iodoform acts first upon the nerve-centres, and finally upon the trunks of the nerves and upon the muscles. After very large doses there is albuminuria and even hæmaturia.

After death from iodoform, a very wide-spread, fatty degeneration is to be found. This change appears to commence in the liver, and to rapidly involve all tissues of the body. M. Floucaud (*Thèse de Montpellier*, 1872) states that there is a very distinct alteration of the blood-corpuscles.

By the alimentary canal iodoform is absorbed very slowly; from wounds it is taken up with comparative freedom. Zeller believes (*Zeitschrift für Physiolog. Chemie*, Bd. viii. 70) that there is always an albuminous compound of iodine formed at the seat of absorption. The iodine escapes from the body by all the secretions as well as by the breath, partially as an iodide, partially as an iodate, and partially in the form of a new organic compound of iodine.* According to the researches of M. Rummo, the elimination of iodine commences within one hour after the stomachic ingestion of the iodoform, and goes on so slowly that the haloid can be found in the urine three days later.

It is probable, as Prof. Binz teaches, that iodoform acts by liberating iodine in contact with the tissues, since Moeller has found that the iodates and iodic acid cause similar symptoms (*Inaug. Diss.*, Bonn, 1877), and Dr. Schwerin has shown that *methyliodide* is also anæsthetic and hypnotic (*Centralb. f. Med. Wissensch.*, 1884, 146).

When iodoform is applied in strong solution, or in substance, it acts as a very powerful local anæsthetic. Thus, a suppository containing it, if introduced into the rectum, will so benumb the parts that defecation may take place without the person or animal being aware of it.

THERAPEUTICS.—Iodoform has been used internally as an alterative and analgesic in *syphilitic rheumatism* and *night-pains*, and in other forms of *neuralgia*. Dr. Stiles Kennedy highly commends it (*Med. and Surg. Rep.*, Jan. 1870, p. 50), and Lazansky finds it very useful in some cases (*Centralb. Chirurgie*, 1876, 219), but that it fails in others; he gives ninety grains a day. Dr. J. Moleschott (*Lond. Med. Record*, Nov. 1878) praises it most highly as an absorbefacient, affirming that by its use he has obtained absorption of various lymphatic tumors, pleuritic, pericardiac, and other effusions, and has even cured acute *hydrocephalus* and *leukæmia*. He relies especially upon its external employment in the form of a collodion (1 part of iodoform, 15 of elastic collodion). So soon as the collodion has dried, he covers it with a film of solution of gutta-percha. Dr. Von Hoffer has used it hypodermically (three to five grains a day) in syphilis, and claims that so employed it greatly increases the number of the red corpuscles. Dr. E. Thomann also bears testimony to the value of these hypodermic injections in secondary syphilis (*Centralb. f. Med. Wissen.*, Oct. 1881). Iodoform, however, has not come into general use, and, in the extensive trials made with it at the Philadelphia Hospital, has failed to sustain its first reputation in syphilitic disorders.

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* For an important bibliography, see the paper of M. Rummo. For details as to elimination and discussion of methods of finding the iodine in the urine, consult Johannes Grundler, *Schmidt's Jahrb.*, Bd. ccii. 232; Prof. Harnack, *Berlin. Klin. Wochens.*, 1883, No. 47, also *Zeits. f. Physiol. Chem.*, viii. 158, 1884; A. Zeller, *Arch. f. Klin. Chir.*, xxviii. 590; Dr. E. Baumann, *Schmidt's Jahrb.*, Bd. ccii. 233; *Verhandl. Deutsch. Gesell. f. Chemie*, Berlin, 1882, xi. 219.

Whatever position iodoform may finally acquire as an internal remedy, there can be no question as to its value when employed locally. It is useful in cases of painful *ulcers*, even when they are *cancerous*,* serving to alleviate pain and to promote cicatrization. At first employed especially in *syphilitic affections*, it is now found to act equally well in *indolent leg-ulcers* and other non-specific abrasions, and is thought to act not only as a local anæsthetic, but also as a decided stimulant to nutrition. Within the last few years it has been very freely employed in Germany as an antiseptic dressing to wounds, and the testimony is so strong that it is difficult to avoid believing that it is the most certain remedy of this class. It is, however, affirmed to have no power in preventing erysipelas, and used freely is very dangerous to the patients. It is employed either in the form of powder dusted in the wound, or as dressings saturated with it, the first method being at once the more effective and the more dangerous. The quantity required to take life is uncertain. Dr. Langenstein attributes a death to four grammes (*Wien. Med. Wochensch.*, 1882, xxxii. 1051). The cause of death seems, however, doubtful. Dr. Czerny reports death from six grammes, not doubtful (*Ibid.*, p. 180).

ADMINISTRATION.—Iodoform may be applied to ulcers in powder, in solution, or in *ointment* (*Unguentum Iodoformi*—1 to 10, U. S.). When there is a great deal of pain, especially if there be much discharge, the powder may be preferred. In *uterine cancer*, in painful *hemorrhoids*, cacao butter suppositories, containing from five to ten grains of the drug, should be employed. Owing to the bad odor of the drug, its application about the mouth and throat is often objected to. According to Dr. Lewis Elsberg (*Phila. Med. Times*, Oct. 4, 1873, vol. iv. p. 4), if to four parts of absolute ether (Squibb's) one part of crystallized iodoform be added, and the whole shaken in a *red* glass flask, a solution is obtained of sufficient strength for effectual use in diseases of the mouth, and free from odor other than that of ether.

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* Consult papers by Dr. G. Völker (*Bulletin de Thérapeutique*, t. lxxiii., Dec. 1867) and Dr. Féréol (*Ibid.*, t. lxxiv., May, 1868). The surgical reader may consult with advantage the following additional references: *Corresp.-Blatt f. Schweiz. Aertz.*, 1882, xii. 609; *Deutsch. Med. Wochensch.*, Berlin, 1882, viii. 146; *Centralb. f. Chirurgie*, viii. 755, ix., various papers; *Journ. Méd. de Bordeaux*, xi. 205; *Allgem. Wien. Med. Zeitung*, 1881, xxvi. 455; *Wien. Med. Presse*, 1882, xxiii. 201.

OLEUM MORRHUÆ—COD-LIVER OIL. U.S.

Cod-liver oil is obtained from the liver of Gadus morrhua and other species of Gadus. In the manufacture of the so-called *shore oil*, the only variety usually employed in medicine, the fish caught near land are brought at once to the shore, and the oil is obtained from the fresh livers by one or other of several processes. The original custom was to put the livers into large kettles, add water, boil to a pultaceous mass, drain off the liquid, allow it to stand, and finally to skim the oil as it rose to the top. A more modern method is to heat the livers by steam applied to the outside of the vessel containing them, to allow drainage, and to proceed as in the process just described. I am informed that at present some of the finest brands of oil are prepared by forcing currents of steam at high pressure through the mass of livers, tearing them in this way to pieces and melting out their oil. *Shore oil* should be a perfectly limpid, yellow, thick oil, free from rancidity, and having the peculiar taste and smell of the oil well developed. *Straits oil* or *Banks oil* is prepared from those fish caught at the "Banks," far from land.

The livers are thrown into casks and allowed to stand for a greater or less length of time and to undergo more or less complete putrefaction, until, on the return of the fishing-smack to port, they are thrown into water-boilers and treated in a manner similar to that previously described. Of straits oil there are two varieties: the *brown* oil, which is much darker than shore oil, and much more nauseous to the taste and smell; and the *black* oil, which is very dark, and still more disgusting in its evidences of rancidity. Both of these varieties are largely used in the preparation of leather.

When a mineral acid (especially the sulphuric) is added to cod-liver oil, the well-known biliary play of colors occurs; but this does not prove the genuineness of the drug, or demonstrate that it is derived from the codfish: it only shows that it is a *liver* oil. It is scarcely to be doubted that not rarely the livers of other fish are largely mixed with those of the Gadus morrhua, but it is not probable that this often happens to such an extent as to interfere with the therapeutic value of the product: indeed, it is far from certain that cod oil is really superior to that produced by the same organ of other fishes. Be this as it may, the physical properties afford the only known test as to the genuineness of the drug. Cod-liver oil is a very complex substance, containing, according to the analysis of De Jongh, glycerine, oleic, margaric, butyric, and acetic acids, gaduin, various biliary principles, such as fellinic, cholic, and billifellinic acids, iodine, chlorine, traces of bromine, phosphorus, phosphoric acids, and various other substances. According to the U. S. Dispensatory, the proportion of iodine never exceeds one part in two thousand. In De Jongh's analysis the greatest amount was found in the light-colored oils, and was only four-hundredths of a grain in one hundred grains of the oil. *Gaduin* is a peculiar, dark-brown substance, which is probably medicinally inert. When to cod-liver oil ammonia is added, there can be obtained, by distillation, a peculiar ammoniacal base, *trimethylamin* (commercial *propylamin*), which exists in no other officinal oil, but occurs in the ergot.

PHYSIOLOGICAL ACTION.—As is well known, all fatty substances when taken into the system have a tendency to cause deposition or formation of fat in the body. Cod-liver oil certainly shares this property in an eminent degree. Dr. Pollock, as quoted by Prof. Stillé, has found that if there be given of it to pigs from one to two ounces *per diem*, to sheep one ounce, and to bullocks from three to nine ounces, it is digested, and aids in fattening the animal; larger amounts than those noted, in Dr. Pollock's experiments, always deranged very seriously the digestive function. No close studies of the effect of cod-liver oil upon healthy men have, that I am aware of, been made. Undoubtedly it tends to produce obesity; but, as no other oil is able to supply its place in various chronic diseases, it must have some influence upon nutrition not shared by ordinary fatty matters, and therefore is an *alterative*.

The history of the clinical use of oleum morrhuæ certainly indicates that it influences the constitution of the blood. It is an every-day occurrence to see pale, anæmic patients become, whilst taking it, rosy and plethoric. According to the analysis of the blood of a patient made by Simon, there is, during its use in phthisis, a great increase in the amount of solids in the blood, a diminution of the fibrin, and an increase in the albumen. The examinations of Dugald Campbell (*British and Foreign Med.-Chir. Review*, 1856, vol. xvii. p. 21) have confirmed the results of Simon. It is very probable that cod-liver oil has some peculiar influence upon the blood-making organs. Upon the various single functions of the body, except the digestive, cod-liver oil has no apparent immediate effect, disturbing directly neither the nervous, motor, respiratory, circulatory, nor secretory movements. When by its use the general nutrition is improved, all the functions seem to share equally in the improvement. Cod-liver oil has undoubtedly, when given with sufficient freedom, a tendency to cause indigestion and looseness of the bowels. All oils are of difficult digestion, and when too much of the oleum morrhuæ is exhibited in man, as in animals, it exerts a deleterious local effect upon the alimentary apparatus.

Much speculation has been indulged in as to which of its ingredients cod-liver oil owes its peculiar medicinal properties. Certainly, however, no real light has been shed upon this matter, and the present probabilities are that it acts as a whole,—*i.e.*, that its virtues depend upon the peculiar combination.

If the experiments of Dr. Oswald Naumann (*Archiv der Heilkunde*, 1865, p. 536) be as accurate as they appear, he has certainly proven that cod-liver oil has physical properties which must aid in its usefulness, although it is not probable that its value depends solely, or even in great part, upon them. He first tested the rate at which various oils pass through fresh moist animal membranes when pressed upon by a column of mercury or by the weight of the atmosphere over an exhausted receiver, and found that cod-liver oil passed much more rapidly than any of a number of oils tried. Apparently this power depended in some measure upon the presence of the biliary principles, since if it was deprived of them the rate of its passage was greatly lessened, but was again increased by the addition of a little bile. The investigator then, opening the abdomen of cats, separated in each animal by ligatures two knuckles, of equal length and entirely similar, from the remainder of the intestines. Into each of them he injected a certain amount of bile, and then into one ordinary oil, into the other cod-liver oil; and when the animals died, some hours afterwards, it was always found that much more of the oleum morrhuæ was absorbed than of the other oil. These experiments were, unfortunately, too few and incomplete to be decisive, but certainly they indicate that the oleum morrhuæ is more easily and rapidly absorbed than other animal oils. The superior fitness of the oil for absorption is in accord with the clinical observation of M. Berthé (*L'Union Méd.*, x. 1856), that cod-liver oil could be taken longer than other fats without appearing in the fæces, and is confirmed by Prof. Bucheim (*Arch. Exper. Path. u. Therap.*, Bd. iii.) as well as by J. Gad (*His and Braune's Archiv für Anatom.*, 1878). Both Bucheim and Gad believe that this absorbability depends largely upon the presence of free fatty acids in the oil.

Dr. Naumann's last series of experiments were directed to discovering the comparative ease with which animal oils and the cod-liver oil were oxidized. For this purpose he used a test solution of the permanganate of potassium, and on adding to given bulks of this, in test-tubes, equal amounts of the various oils, noted the changes of color induced by the reduction of the permanganate. He found that cod-liver oil was the first to be affected. It is evident that the power of being easily absorbed and easily oxidized fits a fat for use in the animal economy; but the peculiar value of oleum morrhuæ does not depend solely upon these properties.

THERAPEUTICS.—Cod-liver oil is especially useful in that condition of system in which, with general lowered tone, there is a tendency to cellular hyperplasia, to the formation of "exudations" composed of imperfectly-developed cells, which, in the great majority of cases, from the very beginning are incapable of development into perfect entities, having only one potential quality, that of dying. There are various types of this diathesis, or condition of system. In one of them there is a tendency to increase in the lymphatic glands; to multiplication, at the expense of development, of their cellular elements,—*i.e.*, to the formation of numerous imperfectly-developed cells, and, finally, to the destruction of them. The death of these cells is partly due to their inherent qualities, and is partly the result of the pressure which they exert upon one another and upon their sources of food-supply

If they undergo a slow, fatty degeneration, with desiccation, cheesy deposits are formed; if a rapid, fatty change, with abundance of moisture, pus and abscesses are produced: in either case, ulceration is the final result. This is the so-called scrofulous diathesis,—*scrofulosis.* In another of this group of diatheses, the tendency to cellular hyperplasia affects the mucous membranes of the air-passages, and the patient, on the slightest provocation, suffers from catarrh, until finally a multiplication of cells occurs so rapidly as to fill up a greater or less number of the air-vesicles of the lungs, generally those of the apex, and "*consumption*" results; or else, an attack of pneumonia being produced by some exposure, the exudation is cellular rather than fibrinous, and catarrhal pneumonia, ending in the majority of cases in a more or less rapid phthisis, occurs.

As already stated, it is especially in these conditions of system that cod-liver oil is so extremely useful. Preceding the development of active disease in these cases there is very generally a recognizable stage, marked by weakness, a tendency to emaciation, more or less anæmia, and other symptoms, which the present is scarcely the place to consider in detail. In this stage, cod-liver oil is exceedingly efficacious, and its use, combined with proper hygienic measures and the exhibition of other suitable drugs, may often succeed in warding off fatal disease. In *scrofulosis*, it is useful in all stages, but should never be relied on to the exclusion of other drugs. Its effects are more marked during the *ulcerative* and *suppurative stages*, but in most cases it aids iodine very materially to reduce the enlarged glands in the earlier periods of the disease.

There are various diseases of the bones, dependent upon or resulting from a scrofulous taint, which are most favorably affected by cod-liver oil. Sometimes the disease attacks the articulating surfaces, giving origin to chronic inflammations of the joints,—*white swellings;* sometimes it is the body of the bones, especially of such as are composed chiefly of spongy tissue, that is affected, and *caries*, with subsequent abscesses, results. In these, as in all other forms of scrofulosis, cod-liver oil is almost a specific. An affection probably not identical with, but closely allied to, scrofula, is *rickets;* cod-liver oil is of great value in this complaint. In certain pale cachectic children there may be found a swollen, tumid belly, perhaps with evident enlargement of the liver, and very generally, if not always, with enlargement of the mesenteric glands. This is the so-called *tabes mesenterica*, which is sometimes relieved, or even cured, by the exhibition of cod-liver oil.

The value of cod-liver oil in what is often very incorrectly called the "*pre-tubercular*" stage of phthisis has already been alluded to, but is so important that it will bear reiteration. There can be no doubt that consumption often commences with catarrh, and is often developed slowly as the result of frequently "catching cold." Whenever a patient is feeble, pale, somewhat anæmic, complains of his liability to catch cold on the slightest exposure, even though no local disease exists anywhere, or rather because no local disease exists anywhere, there is cause for alarm; and it is of the most vital importance that the patient be put upon a tonic treatment whose basis is cod-liver oil, be fed upon nutritious diet, and have the hygiene of his daily life regulated, especial care being taken to avoid any exposure to cold. In the advanced stage of chronic *phthisis* the remedy is less efficacious, in that it much more rarely effects a cure than in the pre-tubercular stage; yet it does more good than all the other remedies of the Pharmacopœia combined, —alleviating the cough, increasing the strength, weight, and general health of the sufferer, often retarding or even arresting the pulmonic disorganization, almost always greatly prolonging life, and sometimes, in conjunction with other measures, effecting a cure. It is a question of some importance to decide how the remedy does good in these cases. Its value, before the occurrence of any lesion, as a preventive of consumption, indicates that its influence during phthisis is not directly upon the local lesion, but upon the general condition of the system. This inference is borne out by clinical experience. The general symptoms commence to improve before the local lesions, and sometimes, although the patient fattens and gets stronger for a time, the pulmonic affection steadily increases; again, in some instances the oil fails to increase the weight of the patient or sensibly to affect the general nutrition, and in these cases it never does any good. In true *tuberculosis*, cod-liver oil, like all other remedies, is of very little, if any, value.

In cases of *defective nutrition*, when pallor, anæmia, loss of strength, and, perhaps, emaciation, occur without any obvious cause, cod-liver oil is often of great service, especially when the subject is a child. Indeed, in children these symptoms are simply the result of a very mild action of the same depressing causes whose more intense malign influence produces scrofula.

In persons broken down with any of those chronic diseases which take the form of a dyscrasia, the remedy is often of great service. Thus, in the cachexia of *tertiary syphilis* it is invaluable. The disease by whose relief and cure cod-liver oil first achieved its reputation is *chronic rheumatism*. I think, however, that it is much more efficacious in those cases in which the rheumatic disease has been grafted upon a scrofulously-tainted constitution, or in those cases in which the patient has been broken down by the disease, or by other agencies, so that there is what may be styled a general nutritive dyscrasia, than in simple chronic rheumatism; yet in obstinate *sciatica* and *lumbago* trial of it should always be made. In *gout*, oleum morrhuæ is of little service, and should be used only in the very chronic form of the disease, and when there is a generally disordered nutrition.

In *nervous affections*, especially in *neuralgia*, in *skin-diseases*, in fact, in any chronic disorder in which the patient is feeble and presents a condition of general depraved nutrition somewhat similar to that seen in consumption, cod-liver oil may be exhibited with advantage.

ADMINISTRATION.—The dark oil has been esteemed most highly by some authorities, especially by De Jongh, who asserts that it contains more of the biliary principles than does the pale oil, and even believes that the products of decomposition in it increase its beneficial action. It is, however, never employed at present, because of its exceedingly repulsive taste, and because it is very prone to disagree with the stomach. One of the difficulties in the use of even the pale oil is the very common real or imagined inability of the patient to take it. Without doubt, this very often arises from its nauseous taste, to lessen or disguise which various expedients are resorted to, with more or less doubtful success. Sometimes a piece of salt taken into the mouth just before the oil, which is also immediately followed by another lump of salt, suffices. It is said that some prefer the oil in emulsion made with some strong aromatic water. The addition of an equal part of glycerine and a half to one drop of the oil of bitter almonds to the dose certainly lessens the taste of the medicine. Some patients take it best in the froth of ale or porter, the glass being first half filled with the malt liquor, then the oil being carefully floated on the top of it without touching the sides of the glass, and the remainder of the vehicle put upon the top of it. Most of the patients requiring oil are also benefited by the use of alcohol; and my experience with the remedy is that the most generally successful plan of exhibition is to place, according to the exigencies of the case, from one to three tablespoonfuls of whisky or brandy in a tumbler, add not so much water, put the oil in the centre, and *toss* the whole down the throat, the head being held well back, the mouth wide open, and the lips not touched by the medicine. The stimulus of the alcohol often enables the stomach to digest the oil when otherwise it could not do it. Sometimes it is necessary to commence with a single small daily dose, even a single teaspoonful, which is best taken at bedtime, and gradually to increase the amount as the patient becomes habituated to it. Children almost always learn to tolerate the taste of the oil, or even become in a short time fond of it. The usual dose is for an adult a tablespoonful three or four times a day; for a child one year old, a teaspoonful. When infants cannot tolerate cod-liver oil by the mouth, inunctions may sometimes be practised with advantage. Drs. N. A. Randolph and A. E. Roussel state that they have seen in such cases the oil appear in the fæces (*Philad. Med. Times*, xiv. 239).

ACIDUM PHOSPHORICUM—PHOSPHORIC ACID. U.S.

Phosphoric acid, which results from the burning of phosphorus in the air, is prepared by the action of sulphuric acid upon bone-ash, which consists chiefly of the phosphate of calcium. The officinal acid is the tribasic acid of chemists. *Acidum Phosphoricum Dilutum*, U. S., contains twenty per cent. by weight of the stronger acid. It is a colorless, inodorous, sour liquid, of a syrupy consistence, which has a very acid reaction, but is not corrosive to animal tissues. The bibasic pyrophosphoric acid is said to be a cardiac sedative (*Journ. Anat. and Physiol.*, xi.).

THERAPEUTICS.—Phosphoric acid has been used to a considerable extent abroad as a tonic and alterative in *scrofulous affections*. Upon the digestive organs, in my experience, it has little or no effect, and I have never been able to perceive that it is at all astringent or exerts any alterative influence upon the glands of the alimentary canal. In scrofulosis and rickets it is, I think, inferior to the phosphates.

PHOSPHATE OF CALCIUM.—The phosphate of calcium is, as is well known, an essential ingredient of bones, of which, indeed, according to the analysis of Berzelius, it forms more than fifty per cent. (*Traité de Chimie*, Paris, 1833). It should not be forgotten, however, that it exists in notable quantities in all the tissues, and is probably as essential an ingredient of their structure as of that of bone. Whenever it is taken out of the food of animals, although they be otherwise well fed, sooner or later they waste, sicken, and die. Chossat fed pigeons exclusively on corn containing very little of the phosphate of calcium, and found that after some months they wasted, were affected with diarrhœa, and died (*Comptes-Rendus*, t. xiv.). According to Roloff (*Virchow's Archiv*, Bd. xlvi. p. 302), a herd of cows which had been fed upon hay from a certain meadow were very much out of health, and suffered from *fragilitas ossium*. On examination, the hay was found to be nearly free from earthy salts, and upon bone-meal being given to the cows they recovered their health in four weeks. The same authority further states that, in some meadows with which he is acquainted, the disease is endemic among the cows because the grass is so poor in phosphates. Haubner also affirms (*Schmidt's Jahrb.*, Bd. cli. p. 138) that cattle fed exclusively upon potatoes, or upon roots very poor in phosphates, fail to fatten, become weak, and are apt to suffer from caries, but that if the phosphate of calcium is given they rapidly improve; and E. Voit (*Zeitsch. f. Biologie*, xvi. 198) states that rachitis without emaciation can be produced in three or four weeks in young dogs by taking the phosphate of lime out of the food. Hegar (*Schmidt's Jahrb.*, Bd. cli. p. 138) has considered the absorption of the phosphate of calcium, when given as a medicine, very doubtful, because when he exhibited it freely there was no increase in the amount of the phosphoric acid or of the earthy bases in the urine. Böker (*Ibid.*), on the other hand, has found that if the drug be given to those wet-nurses whose milk contains an abnormally small amount of phosphates, the milk soon becomes rich in the earthy salts, and L. Perl (*Virchow's Archiv*, lxxiv. 54) has found that administration of the phosphates is followed by an increase in their amount in the urine. Further, Albert Riesell (*Hoppe-Seyler's Medicin.-chem. Untersuch.*, p. 318) has shown that the phosphates are eliminated by the intestines, and therefore that even if it were a constant fact that their renal excretion is not augmented by their administration, it would not prove that they are not absorbed. M. Teissier has found that in the early stages of phthisis there is a very great increase in the excretion of the earthy phosphates by the kidney (*Le Mouvement Méd.*, Sept. 1875), and the researches of Prof. Beneke[*] (*Schmidt's Jahrb.*, Bd. cli. p. 138) are said to have shown that this increased renal elimination, which plainly occurs in several allied diseases, is not accompanied by any increase in the amount ingested in the food, or decrease of the amount eliminated by the intestines, and that, consequently, there is a very decided wasting of the normal phosphates of the body. This being so, the use of phosphates in these diseases is as rational as that of iron in anæmia.

THERAPEUTICS.—According to Dusart (*Archives Gén.*, 6e sér., t. xv.), to Beneke (*loc. cit.*), and to Teissier (*loc. cit.*), the diseases in which the phosphate of calcium is especially indicated are *rachitis*, *osteomalacia*, *phthisis*, and *scrofulosis*. It is evident that the indications for the earthy salts are very strong in the first two of these affections; and clinical experience has certainly borne out the results of *a priori* reasoning. In *scrofulosis*, the call for the drug is not so plain; but Prof. Beneke states that in many cases, if the urine be examined, it will be found to be abnormally rich in earthy phosphates, and that under these circumstances the remedy is of the greatest value. Cases are not rare of children of slow development, often seemingly well nourished and robust, and yet really pale and with flabby flesh, but without any distinct symptoms or marks of scrofulosis or of rachitis. Under these circumstances, the child is in a condition allied to that of the diathesis spoken of, and of the value of the phosphate of calcium I have no doubt. In cases of *delayed union* after *fracture*, the present remedy is seemingly indicated, especially since Dusart (*loc. cit.*) has experimentally proven that when given to animals whose bones have been broken it hastens union and makes the callus abnormally heavy and firm. The phosphate of calcium has been recommended in various diseases other than those mentioned, but its value is much more doubtful. Bennett commends it in *chronic phthisis;* Piorry (*Journ. de Chim. Méd.*, t. ix., 1863), in *syphilitic periostitis;* Beneke, in *syphilitic gummata;* Schönian, and also Kugelmann, in the *menorrhagia* of anæmic women. Prof. Beneke calls attention to the use of it during *pregnancy*, and believes that it exerts an influence on the fœtus, so that women who have borne, it may be, only rachitic or scrofulous children will bring forth healthy offspring.

ADMINISTRATION.—The U.S. Pharmacopœia recognizes the *Precipitated Phosphate of Calcium* (*Calcii Phosphas Præcipitatus*), a white, inodorous, tasteless powder, which is prepared by dissolving bone-ash in muriatic acid and precipitating with ammonia. This may be employed in doses of ten grains three or four times a day, but, owing to its insolubility, is not so useful as the so-called *lacto-phosphate of lime.* This preparation, originally suggested by Dusart and Blache (*Archives Générales*, t. xv. p. 67), is made by the action of lactic acid upon the phosphate of calcium, and was found by those experimenters to be soluble in all proportions, not only in water but also in the gastric juice. There is prepared by the druggists in this city an emulsion containing fifty per cent. of cod-liver oil and two grains of the lacto-phosphate of lime to the drachm, which has appeared to me to be the best of all the alterative preparations in cases of the character spoken of in the section on therapeutics. It certainly is very often more easily digested than the pure oil. The dose is a teaspoonful to a tablespoonful, or even more, according to the age.

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[*] I have not had access to the original memoir of Beneke, *Zur Würdigung des Phosphors Kalkes in physiolog. und therapeut. Beziehung*, Marburg, 1870.

Under the name of *chemical food*, or *compound syrup of the phosphates*, a very complex preparation has been much used in disorders attended with impaired nutrition, such as the lacto-phosphate of lime has been recommended in. I have had no experience with it, but very much doubt its being superior, or even equal, to the latter drug.

COLCHICI SEMEN—COLCHICUM SEED. U.S.
COLCHICI RADIX—COLCHICUM ROOT. U.S.

Colchicum autumnale, or *meadow saffron*, whose products the above drugs are, is a little plant growing in Europe and England. It is not really the root which is officinal under the name of colchicum root, but the thickened swollen end of the stem, with the little bulblet whose office it is to develop a new plant. This *corm* is solid and fleshy, an inch and a half to two and a half inches in length, with a longitudinal groove, having a nail-like process (the bulblet) at its base. In the shops it is very commonly kept in transverse slices, which are notched and cordate; the taste is bitter, hot, and acrid. Colchicum seeds are nearly round, about an eighth of an inch in diameter, and of a bitter, acrid taste. The active principle of both seed and corm is an alkaloid, *Colchicia*, whose individuality was first made out by Geiger and Hesse. According to Hübler, it is slowly soluble in water, readily so in alcohol, and not at all so in ether: with concentrated nitric acid it makes a violet solution, which when diluted with water becomes yellow; with concentrated sulphuric acid it strikes an intense yellow. By the action of mineral acids and by other agencies it is resolved into a brownish-green insoluble resin and a crystallizable neutral. substance, soluble in water, *Colchiceina*.

Physiological Action.—When taken in dose of sufficient size, colchicum acts upon man as a poison, producing repeated, uncontrollable vomiting, with nausea and retching, and also violent purging of at first serous character; afterwards the passages become smaller, more mucous, with flakes in them, and finally in some cases bloody. Abdominal pain may be absent or present, but if present is generally griping; sometimes there is gastric burning. Nervous symptoms have been prominent in some of the severe cases. In one instance, it is said, a feeling of numbness or prickling was complained of by the patient; but this seems not to be common. Spasms are very frequent, and sometimes convulsions, which may be fatal, are present. Muscular pains are not rarely experienced, in some cases replacing the spasms, and probably in all other cases coincident with them is great muscular weakness, amounting, as death approaches, to paralysis. Finally, a condition of collapse develops itself, the circulation fails more and more, the pulse, which has been frequent and feeble, becomes rapid and thready, the skin cold, pale, or livid, bedewed with sweat, and death from exhaustion results. Consciousness is preserved until the last. The effect of lethal doses of colchicum on the urinary secretion varies; sometimes the kidneys seem to be nearly unaffected almost to the last; sometimes their functional activity is decidedly increased, but in other cases it is diminished, and even suppression of urine has been noted. The symptoms produced by the largest therapeutic doses of colchicum are slowing of the pulse, nausea, vomiting, abdominal uneasiness, borborygmi, and free purging, together with a sense of prostration and of weakness. The occurrence of the inflammatory changes after the hypodermic injection of colchicia proves that the irritant principle of colchicum acts by absorption, and that the intestinal symptoms are not simply due to a local action,—deductions confirmed by the chemical experiments of Aschoff, who found colchicia in the liver, kidneys, heart, lungs, and blood of a rabbit poisoned with one and a half grains of it.

Upon most animals colchicum acts very much as it does upon man, in poisonous doses producing, as prominent symptoms, severe and often bloody purging, vomiting, great prostration, embarrassed respiration, finally more or less pronounced paralysis, and death, not rarely preceded by convulsions. Reflex actions are lessened, and finally abolished (Albers, Rossbach), in the frog; but Rossbach affirms there is a precedent stage of convulsions with excessive reflex activity; in warm-blooded animals this first stage of excitement is rarely, if ever, seen. According to the elaborate experiments of Rossbach, the motor nerves and the striated muscles are not affected by the poison, but the higher nerve-centres, the spinal cord, and the peripheral sensory nerves suffer palsy. The same observer found that the circulation was very little influenced, that the pneumogastrics were not affected until near death, that the splanchnic and intestinal vagi escaped altogether. In no case do reflex spinal convulsions occur at any time.

A curious fact noticed by Schroff, which shows that colchicia really has little direct influence upon the nervous system, is that the rapidity of death is not at all in proportion to the size of the dose. Thus, in his experiments, the fatal result occurred in rabbits after one and a half grains of the alkaloid, in fourteen hours; after fifteen grains, in eleven hours. This fact, which has been confirmed by Rossbach (*Pharmak. Untersuch.*, Bd. ii. p. 24), seems to be explicable only by the supposition that colchicia kills chiefly by its irritant action on the alimentary canal, and, not being in any dose corrosive, requires time to work out the fatal result, through the instrumentality of a gastro-enteritis. This deduction is confirmed by the long-protracted course of the poisoning after small doses. Thus, Aschoff noted death on the ninth day in a pigeon which had received one-fourth of a grain of the alkaloid.

After death from colchicum, the blood is generally found very dark and imperfectly coagulable; but whether this is due to a direct action of the poison, or is the result of the slow death by asphyxia and exhaustion, is uncertain. The chief changes are, however, in the alimentary canal, the mucous membrane of which is much swollen, intensely congested, sometimes ecchymotic, or with blood free in the intestine.

Geiger (*Annal. Chem. Pharm.*, vii. 274), Hoppe, Aschoff (*Vierteljahresschrift für Prakt. Pharm.*, vi.), Schroff (*Oester. Zeitschrift f. Prakt. Heilk.*, 1856), and Albers (*Deutsches Klinik*, 1856, xxxvi.), have experimented with *colchicia*, and have shown that it causes symptoms similar to those produced by colchicum,* of which it is without doubt the active principle. The closer studies of Schaitanoff, Rossbach, and Paschkis (*Schmidt's Jahrb.*, Bd. cci. 232) appear to have yielded contradictory results. Schaitanoff and Paschkis found that the alkaloid notably increases the arterial pressure; Rossbach, that the circulation is but little affected; whilst in Rossbach's experiments there was a narcosis which seems to have been replaced in the experiments of Paschkis by a peculiar loss of sensibility. The last observer noted also that neither the vagi nor splanchnics were affected. All observers appear to agree in stating† that the chief force of the poison is expended upon the alimentary canal, at least in mammals, and that after death, even when the alkaloid has been given hypodermically, the intestinal mucous membrane is found much inflamed, as is also very frequently the inner coat of the stomach. Paschkis has found the normal excitability of intestinal peristalsis by galvanization of the pneumogastric nerve is destroyed by colchicine.

The action of poisonous doses (one to two grains) of *colchiceina* has been studied upon dogs by Dr. Saml. R. Percy. The symptoms are very similar to those produced by colchicia; they are—increase in the frequency of the pulse, severe purging with tenesmus, vomiting, finally great slowing of the pulse and failure of the heart's action, and death without convulsions. The urine, at first increased, was afterwards suppressed. On post-mortem examination, the mucous membrane of the intestines was found highly inflamed, that of the stomach slightly so, and the heart and arteries were filled with black tarry blood, similar to that of colchicine-poisoning. On the other hand, Paschkis asserts that 1.5 grains of colchiceine injected into the jugular vein of a dog produced no results whatever. It is evident the two experimenters had different substances.

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* Dr. R. Lewins's experiments (*Edinburgh Med. and Surg. Journ.*, vol. lvi., 1841) may be used for comparison. He used colchicum.

† Unfortunately, the works of nearly all these investigators are known to me only at second hand. Not having had access to the original papers, I have been forced to depend upon abstracts in various journals.

The main interest to the therapeutist in the physiological study of colchicum, of course, is in regard to its action in small therapeutic doses. The most prominent result of the ingestion of such amounts is gastro-intestinal disturbance, as shown by abdominal uneasiness, colicky pains, borborygmi, loss of appetite, moderate purging, and sometimes nausea,—symptoms differing in degree only from those of poisoning by the drug. Before they come on, however, there is a lowering of the pulse-rate, sometimes as much as twelve beats per minute. Upon the skin the medicine occasionally acts, producing in some cases *diaphoresis*, and it is said that the amount of this action is in inverse ratio to the effect on the bowels. According to Schroff, the one-hundredth of a grain of *colchicia* is rather more than the therapeutic dose, and produces purging, lasting for several days, with griping pains, cerebral distress, a pulse at first lowered but afterwards accelerated, and a secretion of thick lateritious urine. Any nervous symptoms, such as vertigo, headache, muscular weakness, which may be present as the result of the administration of colchicum, are probably sympathetic upon the gastro-intestinal irritation. It is evident that colchicum influences the bowels powerfully, and probably in this way acts as an eliminative. But in the minute doses often used with great advantage in disease, purging does not occur, and consequently increased elimination, if it takes place, must be through the kidneys: great interest therefore attaches to the influence of the remedy upon the urinary secretion. In considering this, the effects of poisonous and of therapeutic doses must not be confounded, for it is very evident that an irritation which causes suppression of urine may, when present in a much milder degree, produce an increased flow.

It seems very certain that in moderate doses, repeated at regular intervals, colchicum very often increases the flow of urine. In 1828, Chelius announced that during its administration in gout the amount of uric acid eliminated is nearly doubled. Dr. R. Lewins (*Edinburgh Medical and Surgical Journal*, 1841, vol. lvi. p. 200) submitted the urine of several persons suffering from gout, taken before and after the administration of colchicum, to Prof. Christison, who found in the colchicum-urine the *proportion* of urea nearly double, and that of uric acid greater* than, that of the other specimens.

In 1852 Dr. Maclagan (*Edinburgh Monthly Journal of Med. Sci.*, 3d series, vol. xiv. p. 24) analyzed the urine of three cases of rheumatism before and after the exhibition of colchicum: in two instances the *proportion* of urea was very greatly increased, that of uric acid slightly so. In the third case the effect just noted happened at first, but not afterwards.

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* Dr. Harley (*The Urine and its Derangements*, Phila., 1872, p. 81) makes the assertion that colchicum diminishes the excretion of uric acid and even the urea: as, however, he does not deem it necessary to give any authority for the assertion, and as he does not appear to have made any elaborate chemical examination himself, not much weight is to be attached to his testimony.

On the other hand, Prof. Stillé states that Graves and Gardner affirm that the urates diminish under the use of the medicine. It is evident that these different results are not so contradictory as they seem, for it is possible that in one case the colchicum may so act as to increase the elimination of urea, in another that of uric acid; and that when one of these is increased the other may be unaffected, or even diminished.

Further, when the medicine purges freely it is very probable that elimination by the kidneys is lessened; and no account of this is taken by any of the observers whose original papers I have seen. Moreover, these observers also all contented themselves with noting the proportion of urea and uric acid in the urine, when it is evident that the mere proportion, unchecked by the absolute amount of urine secreted during the twenty-four hours, is no criterion as to the absolute amount eliminated. Dr. A. B Garrod (*Med.-Chir. Trans.*, 1858, xli. 348) has made a study of the subject in such a way as to avoid this fallacy, and found that in some cases the amount of urea and uric acid eliminated was seemingly lessened, whilst in others it was seemingly increased; on the whole no marked effect was produced. More precise and extended investigations are still needed to settle the question, but there is certainly at present no proof that colchicum in gout materially influences elimination.

The action of the drug upon the urine during health is evidently very closely connected with the question just discussed. Here again we find conflicting and insufficient testimony. Dr. Bird (*Urinary Deposits*, Phila., 1859, p. 354) quotes Prof. Kramer's* experiments as showing that colchicum does not increase the amount of solids eliminated, and intimates that his own investigations had given similar results. Dr. Hammond (*Proc. Phil. Acad. Nat. Sci.*, Dec. 1858), on the other hand, in a series of experiments in which every care to avoid fallacies, by maintaining equality as to diet and exercise, was observed, found that while squill and digitalis only increased the watery part of the urine, both the organic and the inorganic solids were remarkably increased by colchicum.

In regard to *colchiceina*, the experiments of Prof. S. R. Percy (*Amer. Med. Times*, April, 1862, p. 167) indicate, but are much too few to prove, that in gout it increases the elimination of urea and uric acid.

THERAPEUTICS.—Our knowledge of the use of colchicum in disease is purely empirical, based upon clinical experience; and our acquaintance with its physiological action is not sufficient to enable us even to explain fully what experience has taught, much less to guide us in our use of the drug. *Gout* is the one disease in which colchicum is almost universally recognized as a specific. It may be advantageously employed both as a preventive of the paroxysm and to lessen its severity when developed. During an attack of gout, from ten to twenty drops of the wine of colchicum root may be exhibited every four hours until some decided evidence of its action, such as nausea or slight purging, is induced. It should always be borne in mind that although looseness of the bowels may be useful, yet when colchicum purges the gouty patient actively it mostly fails in achieving the desired therapeutic result. Its action is most favorable when its influence is felt chiefly upon the skin and the kidneys. To effect this desired result, it is often well to restrain the tendency of the drug to act upon the bowels, by combining it with opium. This is especially the case in debilitated subjects, in whom anything like over-purgation must be avoided with the most scrupulous care. By large purgative doses of colchicum the paroxysm of gout may often be suppressed; but experience has shown that this use of colchicum is dangerous, the suppression being sometimes followed by serious internal disease, apparently due to a transfer of the gouty irritation. Between the paroxysms, colchicum may be steadily exhibited to the gouty subject in small doses (ten drops of the wine of the root three times a day); and often great advantage is derived from its combination with the iodide of potassium. This combination is especially useful in irregular atonic gout, such as is most frequently seen in women of feeble nervous organization who have inherited the diathesis, but is sometimes present even in robust men. Ten grains of the iodide and ten drops of the colchicum wine may be given three times a day. Speculations as to how colchicum cures gout seem to me useless in the present state of our knowledge: until we know more of the physiological action of the drug and of the nature of the disease, one theory seems as good as another.

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* Kramer's paper was published in *Keller's Archives*, Dec. 1847, and is entirely inaccessible to me.

In *rheumatism*, colchicum has been highly recommended by some, but has never come into such general use as in gout. In the inflammatory variety of the disease it is of but little value, except in purgative doses, and is mostly administered in the form of *Scudamore's Mixture*, which is composed of magnesia and its sulphate with wine of colchicum root. In *subacute rheumatism*, the combination of colchicum and iodide of potassium, already spoken of, is very useful.

Colchicum has been administered in various diseases, but when there is no rheumatic or gouty taint is at present very rarely used.

TOXICOLOGY.—The symptoms of poisoning by colchicum have been already enumerated. The fatal dose varies, but is small. Prof. Geo. B. Wood (*U. S. Dispensatory*, 13th ed., p. 1504) states that death has been produced by two drachms and a half of the wine of colchicum root; and Taylor (*Medical Jurisprudence*, 2d ed., vol. i.) records a case in which three drachms and a half proved fatal. On the other hand, recovery has taken place after the ingestion of an ounce.* According to the experiments of Schroff, *colchicia* is eighty to one hundred times stronger than the fresh corm. According to Heinrich,* 0.15 grain of colchicia will produce poisonous symptoms in man, and in Krahmer's experiments (*Journal für Pharmacodynamik*, ii. 561) 0.3 grain caused in an adult violent serous purging, lasting for four days, and accompanied with severe tenesmus. Casper has seen death result from a quantity of the wine containing 0.025 to 0.03 gramme (0.37 to 0.45 grain) of colchicia; but, according to Husemann, recovery has taken place after the ingestion of 0.045 gramme of the alkaloid. Very recently (Dr. Geo. W. Major, *Canada Med. and Surg. Journ.*, Dec. 1873) seventeen cases of poisoning from one bottle of wine of colchicum seeds occurred in Montreal, seven proving fatal. The patients had been vomiting and purging almost continuously for many hours when first seen, and the symptoms were exactly those of the stage of collapse of severe cholera morbus. In no case was the purging bloody. Consciousness was preserved to the last, and in only one case was there anything like convulsions. There was decided numbness of the extremities; and a peculiar hoarseness of the voice was especially noted.

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* See case in *L'Union Médicale*, Aug. 1848.

The treatment of colchicum-poisoning is as follows. If the stomach and bowels have not been freely evacuated, administer at once an emetic and a cathartic, so as to empty the alimentary canal; allow the patient to drink freely of warm water, to aid in these operations and to act on the kidneys. Give freely of tannic acid, as the only known chemical antidote; although experiments upon animals have shown that it is not to be relied upon. To check the vomiting and purging, administer opium freely; and to allay the irritation, cause the patient to drink freely of albuminous matter, such as white of egg dissolved in water; the tannic acid having been given as soon as possible after the taking of the poison, the demulcents are useful in the more advanced stages. Symptoms of gastro-enteritis or of collapse are to be met as they arise.

ADMINISTRATION.—Colchicum is never used in substance; the wine of the root is deservedly the most popular preparation. Recently it is claimed that colchicia hypodermically administered is especially efficacious in rheumatism; the dose is one-fiftieth of a grain (*Berl. Klin. Wochen.*, 1877, 197).

The officinal preparations from the seeds are: the *tincture* (*Tinctura Colchici Seminis*, 1 to 6.6),—dose, half a teaspoonful to one and a half teaspoonfuls; the *wine* (*Vinum Colchici Seminis*, 1 to 6.6),—dose, half a teaspoonful to one and a half teaspoonfuls; and the *fluid extract* (*Extractum Colchici Seminis Fluidum*),—dose, two to six minims.

The officinal preparations of the root are: the *wine* (*Vinum Colchici Radicis*, 1 to 2.5),—dose, ten to fifteen drops; as a purgative, half a fluiddrachm; the *extract* (*Extractum Colchici Radicis*),—dose, one to two grains; and the *fluid extract* (*Extractum Colchici Radicis Fluidum*),—dose, two to four minims.

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* Quoted by Husemann.

SARSAPARILLA—SARSAPARILLA. U.S.

The root of Smilax officinalis and other species of Smilax, woody vines inhabiting Mexico and the northern portions of South America. There are in commerce a number of varieties of sarsaparilla, the two most important of which are the *Honduras* and the *Brazilian*. The former of these is almost the only sarsaparilla used in this country. It occurs in bundles two or three feet long, composed of several very long, thin roots, folded upon themselves, the whole being bound round by a number of turns of the root. The Brazilian sarsaparilla also comes in cylindrical bundles, each of which is closely wrapped about by a very flexible stem: it mostly has fewer rootlets than the Honduras variety. The crude sarsaparilla has little or no smell, but its taste, which is at first simply mucilaginous, soon becomes, if the root be chewed, persistently acrid. According to Prof. Geo. B. Wood, the degree of this acridity is the best measure there is of the activity of any specimen of the drug. Sarsaparilla contains a crystallizable principle, first discovered by Palotta in 1824. From its discoverer this substance received the name of *Paraglin*. By subsequent authorities it has been variously called *Smilacin*, *Salseparin*, *Sarsaparillin*, and *Parallinic Acid*. Paraglin, according to Poggiale, crystallizes in fine needles; according to Thubeuf, in star-like clusters of plates. It has a neutral reaction, and in solution a bitter, acrid taste, but when solid it is nearly tasteless. It is very slightly soluble in cold water, more so in boiling water; moderately soluble in dilute alcohol when cold, freely so when hot. Palotta asserts that thirteen grains of it cause vomiting, constriction in the throat, weakness, diaphoresis, and depression of the circulation. On the other hand, Böcker, of Bonn, has exhibited it in doses of a like amount without producing any symptoms whatever (*Journ. für Pharmacodynamik*. Bd. ii. p. 23).

PHYSIOLOGICAL ACTION.—It has already been shown that there is very little reason for believing that paraglin has much immediate action on the system; and the question naturally arises, Has sarsaparilla any more influence? The answer to this question must, I believe, be a negative one, since the only sensible effects that follow even the largest draughts of the decoction are simply the results of slight gastric disturbance. It has been claimed that sarsaparilla acts as a diuretic and diaphoretic; but the only record I have met with of any careful experimentation is that of Böcker (*loc. cit.*). That investigation seems to show conclusively that the drug has no marked influence upon these secretions. If, therefore, sarsaparilla have any value whatever in disease, it must be simply as an alterative,—as a remedy which in some unknown way modifies nutrition.

THERAPEUTICS.—Sarsaparilla has been used, and still is used, to such an enormous extent in medicine that it seems impossible to believe that it is destitute of therapeutic virtue. It is not in accordance with the plan of the present work to enter into an elaborate discussion of the recorded clinical experience with it: suffice it to say that, although the evidence is contradictory, on the whole there is a decided preponderance in favor of the value of the drug in *chronic syphilis* and in chronic *scrofulous diseases*. I have used it largely, but always in combination with more powerful alteratives, so that it is impossible to decide how much of the good achieved has been due to its influence. There are two distinct methods or objects of use of sarsaparilla in syphilis: one as an adjuvant to mercury in the secondary stage; one as an adjuvant to the iodide of potassium, or as a sole reliance, in the advanced tertiary cases, especially where the constitution is very much broken down by the disease. It is stated that, in the latter condition, very often during its use the appetite will gradually increase, the spirits rise, the secretions become more and more normal, and the strength grow day by day.

ADMINISTRATION.—Sarsaparilla is never given in substance, but in one of the following officinal preparations:

Decoctum Sarsaparillæ Compositum— Compound Decoction of Sarsaparilla.—This contains sarsaparilla, bark of sassafras root, guaiac wood, liquorice root, and mezereon, and is an imitation of the famous "*Lisbon Diet-Drink.*" The dose is three or four fluidounces three or four times a day.

Syrupus Sarsaparillæ Compositus— Compound Syrup of Sarsaparilla.—This contains sarsaparilla, guaiac wood, pale rose, senna, liquorice root, oil of sassafras, oil of anise, and oil of gaultheria, and is a very popular preparation, on account of its pleasant taste: it affords the only vehicle I know of capable of disguising the taste of the iodide of potassium. The dose of it is one to two tablespoonfuls three or four times a day.

Extractum Sarsaparillæ Fluidum—Fluid Extract of Sarsaparilla.—Dose, half a teaspoonful three times a day.

Extractum Sarsaparillæ Compositum Fluidum—Compound Fluid Extract of Sarsaparilla.—This contains sarsaparilla, liquorice root, sassafras, and mezereon. The dose is a teaspoonful.

GUAIACI LIGNUM—GUAIAC WOOD. U.S.
GUAIACI RESINA—GUAIAC RESIN. U.S.

The wood and the resin of the Guaiacum officinale, a large tree growing in the West Indies. Guaiac wood, or *lignum-vitæ*, is imported in billets, but very generally is kept in the shops in the form of raspings or shavings. It is a very dense wood, the central heart-wood having a dark-olive or brownish-green, and the outer sap-wood a light-yellowish, color. It is inodorous, but becomes somewhat fragrant when rubbed or heated. Besides the resin, it contains an extract which is believed to have medicinal properties.

Guaiac resin is obtained to a slight extent by spontaneous exudation from the living trees; much more largely by boring a hole into the centre of one end of a billet, placing the other end in the fire, and catching the melted resin as it runs out; and still more frequently by boiling the chipped wood in salt and water and skimming off the resin as it rises to the surface. Guaiac occurs in irregular lumps or masses, of a dark reddish-brown greenish color externally, offering a conchoidal fracture with somewhat translucent edges. The odor is feeble, peculiar, agreeable, increased by heat. The taste is at first very slight, but, as the resin melts in the mouth, becomes very acrid and persistent. It is a very complex body, containing three acids, the *guiaconic acid* of Hadelich, the *guaiac acid* of Righini, and the *guaiacresinic acid* of Hlasiwetz, besides *guaiac yellow*, a peculiar resin, and other substances. Landerer asserts that he has found in it a peculiar crystallizable substance, which he calls *guaiacin* (Husemann, *Die Pflanzenstoffe*, p. 1106.)

When a lump of guaiac is freshly broken, it offers a dark, blackish surface, which on scraping or bruising becomes yellowish; on exposure, the well-known greenish tint is acquired, owing to a spontaneous oxidation. The ease with which the resin undergoes oxidation is its most distinctive characteristic. As already stated, the change occurs on simple exposure to the light. According to Wollaston, it is most rapid and perfect in the focus of the violet rays of the spectrum, whilst in the focus of the red rays the original color is regained. Oxidizing or ozonizing agents, such as nitric acid, chromic acid, iodine, bromine, and chlorine, produce this oxidation very rapidly and very thoroughly, the resin acquiring an intense blue color.

PHYSIOLOGICAL ACTION.—Guaiac is believed by some to act as a diaphoretic, to do good by increasing the elimination of the skin; but, as I have not been able to obtain either from medical literature or from the exhibition of the medicine any distinctive proof of its having such action to any marked extent, I have preferred to consider the drug as an alterative. When taken internally, very little sensible effect results, unless the dose be so large as to irritate the stomach.

THERAPEUTICS.—Guaiac has been very largely employed in *chronic syphilis*, in connection with sarsaparilla, and is an ingredient of its most favorite preparations. Guaiac has also had a good deal of repute in *rheumatism*, and in the subacute and chronic forms of the affection is often of service. For an account of its employment as an emmenagogue, see the chapter upon that class of remedies. Guaiac is best administered in tincture, either the simple (*Tinctura Guaiaci*, U. S.) or the ammoniated (*Tinctura Guaiaci Ammoniata*, U. S.). The dose of either of these is from one to two teaspoonfuls, administered, preferably in milk, three or four times a day.

MEZEREUM.—*Mezereon* is the bark of two species of Daphne, native shrubs of Europe. It is a thin, grayish, tough, flexible bark, occurring in long strips folded upon themselves, nearly odorless, but having a very acrid taste. It contains a neutral, crystallizable, bitter glucoside, *Daphnin*, besides a volatile acrid principle. Mezereon is intensely irritant, and its ointment (*Unguentum Mezerei*, U. S.) is used as a stimulant dressing to very indolent ulcers, and to keep blisters sore or to maintain issues. Internally, in small doses it is believed to be an alterative, but is never used except in combination with sarsaparilla. In overdoses it is an active poison, producing severe vomiting, purging, and gastro-intestinal inflammation. Sometimes the symptoms of the poisoning are simply those of collapse, with unconsciousness and other nervous disturbances, such as are seen in children from intense gastro-intestinal irritation (case, *Brit. Med. Journ.*, 1882, vol. ii. p. 521).

SASSAFRAS.—The bark of the root of the Sassafras officinale is believed by some to be an alterative, on, as I think, very slight foundation. It contains some tannic acid, and very largely of a volatile oil (*Oleum Sassafras*), which, on account of its cheapness and agreeable odor and taste, is much used both in medicine and in the arts as a flavor and perfume.

TARAXACUM. U. S.—The root of the common dandelion, Taraxacum officinale, is believed to have the property of altering the action of the liver; although no effect is to be witnessed from a single dose of the drug, however large, other, at least, than some nausea. Diuretic properties have also been ascribed to taraxacum; but the only evidence brought forward to establish this is the vulgar name which the plant bears both in English and in French. If useful at all, it is in those cases of dyspepsia in which there is habitual torpor of the liver, with costiveness. It must be given very freely and continuously for weeks before any good effect is to be looked for. The U. S. Pharmacopœia recognizes a fresh juice *extract* (*Extractum Taraxaci*) and a *fluid extract* (*Extractum Taraxaci Fluidum*), either of which may be used in doses of one or two drachms, administered after meals.

Subdivision II.—Local Remedies.

CLASS I.—EMETICS.

Emetics are those drugs which are employed in the practice of medicine for the purpose of producing emesis, or vomiting. The mechanism of vomiting has been so frequently written upon, and has so little connection with the application of emetics, that it is not necessary here to enter upon an elaborate discussion * of it. Suffice it to state that emesis is the result of a very complicated series of actions, in which the chief expulsive force is supplied by the abdominal muscles and the diaphragm,—the stomach, however, participating in the general contraction, and not being, as some have thought, entirely passive. The exact relations and functions of the various nerves concerned are not, I think, fully made out. It has been generally believed that the pneumogastrics were the afferent nerves, and that, although emetics introduced into the circulation after their section acted, yet irritation of the gastric mucous membrane was not capable of so doing. But Schiff found in his experiments that, even when the nerves were cut in the neck, the introduction of semi-solid food into the stomach gave rise to efforts at vomiting, which were in some cases successful; and Maclagan † has obtained similar results with the sulphates of zinc and copper. Moreover, I have invariably failed to induce vomiting with veratria, even when given immediately after section of the par vagum. Evidently, further investigations are needed.

Vomiting occurs under two provocations, or in two manners. Thus, a mental impression, or a disordered state of the blood, may influence the nerve-centres directly, and emesis, spoken of as *centric*, results; or a peripheral irritation in the stomach itself, or in some other organ, as in the kidneys, may induce vomiting precisely similar in the method of its production to the more ordinary reflex movements; such vomiting is called *reflex* or *excentric*.

Emetics produce their results in both of these methods. Thus, tartar emetic has been believed to affect the centres directly, so as to cause centric vomiting, whilst sulphate of copper has been believed to irritate the mucous membranes of the stomach as to produce reflex vomiting. Recently much doubt, however, has been thrown upon the old views, and it is probable that most emetics have a double influence. Thus, the purging of veratria or of tartar emetic is almost certainly connected with its elimination, and is probably due to a direct action of the circulating poison upon the intestinal mucous epithelium, gland-cells, and peripheral nerves. It seems *a priori* almost a necessity that the vomiting caused by these poisons is produced in the same way as the purging. Dr. D'Ornellas has found that when emetia is injected into the veins of animals the vomiting occurs simultaneously with the elimination of the alkaloid from the gastric mucous membrane, and asserts that Kleimann and Simonowitsch have determined the same thing with antimony.* Further (see page 159), antimony seems to cause vomiting partly by acting upon the centres, partly by irritating the peripheral nerve. Irritant emetics are more prompt than those which chiefly affect the nerve-centres, and act more certainly when the nerve-centres are obtunded, as in *narcotic* poisoning; they always cause less nausea and general systemic disturbance than do the centric emetics.

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* For a very elaborate general discussion on emetics, see Prof. Joseph Carson, *Phila. Med. Times*, June, 1872; also, Dr. D'Ornellas, *Bull. Thérap.*, lxxxiv. 193.

† *The Action of Medicines in the System*, by F. W. Headland, M.D., Amer. ed., 1839, p. 110.

Another evident practical fact is, that whilst centric emetics will act in whatever way they are introduced into the system, the mechanical must be exhibited by the stomach. Thus, apomorphia may be given by hypodermic injection, but mustard must be taken by the mouth.

A very curious property of emetics has been pointed out by Dr. E. Harnack (*Archiv Exper. Path. u. Ther.*, Bd. iii. p. 44), who, as the result of an elaborate investigation, affirms as a law that all specific emetic substances destroy, even when in relatively small dose, the excitability of striated muscular fibre. Dr. Harnack seems to establish the general truth of this; but that it is a universal law seems scarcely probable, and the connection between the two properties is very obscure. According to H. Kobert (*Arch. Exper. Path. und Therap.*, xv. 36), antimony has an effect only when the contact is prolonged.

In regard to the phenomena of vomiting, there are a few points to which it is necessary here to call attention. First of these is the fact that *nausea* always produces, or is accompanied by, muscular relaxation. Vomiting may exist, as from mustard, without much relaxation; but when it is accompanied by much nausea the whole system is as it were unbent, the skin soft and bedewed with perspiration, the pulse soft and feeble, the muscular system limp and incapable of exertion, the mental acts almost suspended. During violent vomiting the blood is driven to the head, so that the whole exterior of the cranium, and probably the interior also, becomes very much congested.

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* Copper has been thought to be a purely mechanical emetic, but the experiments of Brunton and West (*St. Bartholomew Hosp. Rep.*, 1876) show that a peptone of copper injected into a vein causes violent vomiting. Those remedies whose irritant powers are great may still well be considered as "mechanical emetics."

The abdominal circulation is very much affected, and the blood is as it were squeezed out of the portal vein and its tributaries. The matters rejected consist of the contents of the stomach, and, in repeated vomiting, also those of the duodenum. The secretion from the gastric mucous membrane is very much enhanced, and without doubt is more or less modified. Bile in ejecta is to be recognized by the green color and the bitter taste, or more infallibly by testing with the proper reagents.

The indications for the use of emetics are as follows:

1. *To unload the stomach.*—For this purpose they are employed in poisoning; in the existence of crude articles of food or indigestible substances in the stomach; or in the presence of acrid, perverted secretion. The symptoms induced by irritating materials in the stomach are various, and sometimes it requires a good deal of tact or experience to recognize their cause. Among them may be mentioned a feeling of weight or load in the stomach, gastric distress, or severe cramp or spasmodic pains, with or without some nausea and retching. In other cases no local manifestations of trouble may be present. Thus, *convulsions* in children are very frequently the result of gastric irritation, and are at once relieved by emptying the stomach. In adults, *apoplectiform coma* may offer a similar history. Occasionally *urticaria*, or hives, and not rarely severe *headache*, have a similar origin, and require a similar treatment.

2. *To affect the abdominal viscera and circulation.*—Emetics have been recommended by some in *congestions* of the *spleen;* but evidence is wanting as to their power to affect materially other viscera than the liver.

In *congestion* of the *hepatic* and *portal* circulation, not dependent upon organic cause, and in the condition of digestive derangement known as *biliousness*, they are often of service. In *catarrhal jaundice* they may effect much good by causing dislodgment of the mucus plugging the ducts. They have been employed in cases of *biliary calculi;* but the chances of forcing out the calculus by external violence are probably no greater than those of lethal rupture of the gall-bladder.

3. *To dislodge substances from the respiratory passages.*—For this purpose emetics are sometimes used when foreign bodies have found entrance into the larynx; but it is chiefly in *membranous croup* that the present indication is met with. The emetics chosen for this purpose should be such as act with violence without producing much nausea or systemic disturbance; the mechanical emetics are therefore the best.

4. *To produce muscular relaxation.*—The introduction of anæsthesia has rendered the use of emetics to meet this application almost obsolete. Occasionally, however, in *asthmatic* or other *spasmodic affections* of the respiratory organs, emetics are still employed. For this purpose the drugs causing much nausea are preferred. In adults, lobelia is the best; in children, ipecacuanha. Nauseating rather than emetic doses should be employed.

5. *To lessen arterial action and reduce inflammation.*—Almost the sole disease in which advantage can be derived from this use of emetics is acute

bronchitis in its early stages. In very many cases a "cold on the chest" in its outset may at once be subdued by ipecacuanha, or, better still, tartar emetic: small doses should be given at short intervals, to produce continuous nausea, terminating after a time in vomiting. This method of cure is so disagreeable, although very efficacious, that patients will rarely submit to it, unless, as sometimes in the case of public speakers, relief within a short period of time be a matter of great importance. It should be added that the cure is wrought in these cases not merely by the lessening of arterial action, but also by the induction of free bronchial secretion.

6. *To create a shock to the system.*—Under this head may be included several empirical uses of emetics, in which advantage is gained, but in a method which is not very clear. Thus, in epileptic attacks, when the fits have a tendency to recur every few minutes, the unconsciousness persisting, it may be, for hours, emetics will sometimes break up the succession of disordered nervous action. Again, not unfrequently an ague-fit can be set aside by an emetic given just before its expected recurrence.

Contra-indications.—The chief contra-indications to the use of emetics are the existence of congestion of the brain, and of gastric inflammation. Advanced pregnancy, and hernia, whilst they do not positively contra-indicate the use of emetics, should cause great caution to be practiced in their employment.

ADMINISTRATION.—Emetics should, as the general rule, be given in a full dose, so as to avoid unnecessary repetition, and should be administered dissolved in water or in syrup. Their action should be assisted by frequent and copious draughts of tepid water, which also have the advantage of rendering the vomiting less painful. When for any reason protracted nausea is desired, the doses should be small and repeated at short intervals.

Hyperemesis may advantageously be divided into two varieties: first, such as is due to overdoses of depressing centric emetics; second, such as arises from irritation of the stomach, as by mechanical emetics. The treatment of the first of these consists in the enforcement of absolute quiet in the horizontal position, the free use of opium enemata, the application of counter-irritants to the epigastrium, and the use of alcoholic stimulants. The latter should be given in hot water, and should not be too much diluted. I have seen raw brandy arrest at once the most alarming centric emesis, after the failure of other methods. Creasote, chloroform, or chloroform and volatile oils, are sometimes of value in this form of hyperemesis. When excessive vomiting is due to some irritant emetic, the stomach should be thoroughly washed out by large draughts of warm mucilage, opium given by the rectum, a mustard plaster or blister, or, often better still, leeches applied to the epigastrium, and no medicine at all be taken into the inflamed viscus. The swallowing of small pieces of ice is sometimes of service. If these remedies fail, the treatment of this form of hyperemesis soon resolves itself into that of gastritis.

VEGETABLE EMETICS.

IPECACUANHA. U.S.

The root of the Cephaëlis Ipecacuanha, a small, shrubby plant, growing in Brazil, where the drug is gathered by the Indians to be exported in large bales or bags. Ipecacuanha occurs in pieces of two or three lines in thickness, variously bent and contorted, marked on their surface with numerous prominent rings, and composed of an outer, thick, active, hard, and horny cortex, and an inner, light, inert, woody centre. Varieties of ipecacuanha—the *red*, the *gray*, and the *brown*—have been formed from the color of the bark, but the distinction is trivial. The root has very little odor, but the brown powder has a decided and peculiar smell, and in some persons excites sneezing, or even violent asthmatic dyspnœa. The taste is bitter, acrid, and nauseous. The active principle is *Emetia*, an alkaloid first discovered by Pelletier in 1817. The cortex also contains small quantities of ipecacuanhic acid, which is related to tannic acid. Pure *emetia* is a white, uncrystallizable, odorless powder, of a bitter, burning taste, soluble in one thousand parts of water at 50° C. (Lefort), freely soluble in dilute and absolute alcohol, in chloroform and benzole, scarcely so in ether. Its solution in acidulated water, according to Draggendorff, has a decided blue fluorescence. Its salts are, according to Pelletier, uncrystallizable. Concentrated sulphuric acid turns it a dirty brown, nitric acid a yellowish brown. Pure emetia is very difficult to prepare, and, according to Mr. Williams (*St. Bartholomew's Hospital Reports*, vol. v.), only two grains of it can be obtained from an ounce of the root. The ordinary impure alkaloid of the shops occurs in brownish-red, transparent, very deliquescent scales, which are very soluble in water.

PHYSIOLOGICAL ACTION.—Locally applied, ipecacuanha is a decided irritant, manifesting its action not only upon mucous membranes and upon denuded surfaces, but even, when used by inunction, producing an eruption upon the sound skin. According to Dr. Dyce Duckworth, this eruption consists at first of small, discrete pustules, with a rather large areola; afterwards, if the application be persisted in, of large pustules, followed by severe ulceration. When exhibited in small repeated doses to man, it produces malaise, with nausea, and perhaps an increase of the secretions of the salivary glands and of the mucous membrane of the bronchial tubes and of the stomach. In large amounts it causes vomiting, accompanied by only a moderate amount of nausea but by a decided increase of the secretions mentioned above. The vomiting, even when very large amounts are taken into the stomach, is not apt to be severe, nor the prostration marked,—no doubt because the excess of the drug is rejected before absorption. In large doses of emetia, this mildness of action, in all probability, would not occur: certainly animals are readily killed by the alkaloid. Although ipecacuanha was made known in 1649 by Piso, and, although it has been enormously used since its introduction into Europe in 1672, its physiological action is not as yet well made out. That the active principle is absorbed, and that the vomiting is so produced, is shown by the experiments of Orfila (*Toxicologie*, i. 651), and of Drs. Dyce Duckworth, D'Ornellas, and Pecholier, who found that vomiting followed the hypodermic use of emetia in dogs and cats. If it be true, as is affirmed by D'Ornellas, that the emetia produces vomiting much more slowly when thrown into the veins than when given by the stomach, it would seem that the local irritant action of the drug efficiently favors emesis.

According to Dr. D'Ornellas (*Gaz. Méd.*, 1873, p. 537), Merck's commercial emetia in toxic doses (0.03 milligramme) produces in frogs dryness of the skin, swelling of the abdomen, diminution of the circulation and respiration, increased rather than diminished sensibility, muscular feebleness deepening into abolition of voluntary movement, with at first increased and afterwards diminished reflex activity, and finally death from failure of respiration; the heart continuing to beat often for many hours. In mammals the symptoms induced by the poison in large doses are very similar to those just detailed, excepting that emesis is usually violent, but in some cases it is wanting.

Circulation.—The action of the drug upon the circulation has not as yet been clearly made out. Any action upon the heart-muscle must be a very feeble one, since D'Ornellas states that although the frog's heart is finally arrested in diastole, yet it retains often for many hours its irritability. It has been supposed by some that the drug acts especially upon the vaso-motor system, but evidence of this has not as yet been brought forward. Polichronie, it is true, asserts (*L'Ipecacuanha*, Paris, 1874) that dryness and paleness of the intestinal mucous membrane are very apparent in mammals poisoned with emetia, and Chouppe (*Le Progrès Méd.*, 1874, p. 425) has observed the same thing; but this is an absurdly slight ground for believing that emetia causes vaso-motor spasm. Pecholier found in a single experiment that the drug abated very decidedly the arterial pressure, but Dr. D'Ornellas found that emetia neither depresses nor increases the blood-force; and in a series of elaborate experiments by Dr. Dyce Duckworth the alkaloid failed to influence materially the circulation, at least until very late in the poisoning. The pulse-rate was not constantly affected; sometimes it was apparently lowered, sometimes it remained about the same, and sometimes it was seemingly increased. The effect of a toxic dose was, however, marked. In one case immediate suspension of cardiac action followed injection into the jugular vein; in another dog, in a minute and a half after half a grain of emetia, the arterial pressure descended from 135 to 20, and in a moment the animal was dead of cardiac paralysis. Dr. Foulkrod (*Phila. Med. Times*, viii., p. 554) has noticed a steady fall of arterial pressure produced both before and after section of the cord of all the cardiac nerves. There is no proof that emetia ever causes vaso-motor spasm, whilst it is certain toxic doses directly paralyze the heart; therapeutic doses probably have no decided direct effect upon the circulation.

Respiration.—According to D'Ornellas, Pecholier, and Foulkrod, emetia in toxic doses usually kills by arresting the respiration; but in many of Dyce Duckworth's experiments (*St. Bartholomew's Hosp. Rep.*, v., vii.) the death was certainly the result of cardiac paralysis, possibly because the poison was thrown directly into the circulation,—*i.e.*, into the heart.

Nervous and Muscular Systems.—Upon the cerebrum ipecacuanha exerts no perceptible influence; but, as both D'Ornellas (*loc. cit.*, p. 538) and Pecholier (*loc. cit.*, p. 57) have found that after death from emetia in the frog both nerves and muscles retain their susceptibility to feeble galvanic currents, the paralysis which the poison produces is probably spinal. D'Ornellas and Pecholier are in opposition in regard to the action of the alkaloid upon sensibility, the one affirming that it is not, the other that it is, affected.

Temperature.—Pecholier, Dyce Duckworth, and D'Ornellas all state that in emetia-poisoning there is a distinct fall of temperature in the mouth and on the surface of the body, but that in the intestines the temperature either remains stationary or, more commonly, rises; D'Ornellas affirms that it always rises decidedly. This rise is probably, as D'Ornellas believes, local, and due to the action of the poison upon the intestinal tract.

Pulmonic and Digestive Organs.—The post-mortem results obtained in animals poisoned with ipecacuanha are diverse, but affect chiefly either the lungs or the digestive tract. Pecholier, in his earlier experiments, found great paleness of the lungs, with intense hyperæmia of the stomach and the upper half of the intestines, but in some of his later experiments the lungs were profoundly influenced. Dyce Duckworth especially noted intense hyperæmia of the lungs, which were in some places emphysematous, but in other portions collapsed and even affected with true consolidation. The lesions were much less marked in the intestines than in the lungs, which resembled very closely those taken from the bodies of animals killed by section of the vagi. The pulmonic lesions were found to be most intense in the rabbit; the intestinal, in the dog, cat, and guinea-pig. Magendie forty years ago noted the pulmonic lesions of emetia-poisoning, and D'Ornellas has also recorded them, but has also seen cases in which ischæmia of the pulmonary tissue was found after death. It is evident that the poison has an especial action upon both lungs and intestines; but why the pulmonic lesions should so vary is not at present known. The occurrence of changes in the pulmonary tissues is in accord with the results of clinical experience, which teaches most decidedly that ipecacuanha has an action upon the pulmonary mucous membranes. After section of the cervical vagi, Dr. Dyce Duckworth found that emetia failed to cause vomiting.

Clinical experience also shows that ipecac acts upon the digestive tract. Whether given in large or in small doses, it is very apt in man to increase and modify the intestinal secretions. It probably influences the liver, since Pecholier (*Gazette Médicale*, 1862) affirms that in animals killed by it no hepatic glucose can be found. Moreover, great advantage from its use may often be obtained in the condition known as "biliousness." In "bilious dysentery" it will often produce large tarry discharges; and I have seen a change in the color of the stools follow its use in catarrhal jaundice. The mechanical effect of the vomiting induced by it in these cases, however, must not be lost sight of; yet it does not seem to me at all sufficient to account for the results, especially as some observers state that the effects noted are produced even when little or no vomiting occurs. It has been proven by D'Ornellas and Pecholier that when emetia is introduced into the circulation or into the cellular tissue it escapes with the secretions of the stomach and bowels; so that the changes which are provoked in these organs are evidently connected with the elimination of the drug.

THERAPEUTICS.—The most ordinary use of ipecacuanha is as an emetic. Whenever it is desired to unload the stomach or to act by emesis upon disease, without inducing much prostration, this drug commends itself by its safety and efficiency. In *narcotic poisoning* it is less certain than the "mineral emetics," but, as it produces no irritation of the stomach, can be given more freely than they can, and is constantly used as an adjuvant to them. It is especially useful in the diseases of children, never causing the serious depression which tartar emetic is so apt to produce. When, however, very violent emesis is desired, as in *membranous croup*, other emetics, such as zinc or alum, are to be preferred, on account of the greater force of their action.

In *sick stomach* of nervous origin, such as occurs in *pregnancy*, minute doses of ipecacuanha have so often met with success that there can be no doubt of their value. One drop of the wine in a teaspoonful of water should be given every hour. The use of ipecacuanha as an expectorant will be spoken of under that heading.

One of the most important uses of ipecacuanha is in *acute dysentery*,—all forms of which have been treated with it with asserted advantage. I think, however, its beneficial action is best seen in "*bilious dysentery*" and in "*malignant dysentery*," as is indicated by the fact that its use is most common in tropical climates. In "*sthenic inflammatory dysentery*" it seems to be less available; although even in this it has been strongly advocated by some. Dr. Chouppe (*Bull. de Thér.*, June, 1874) commends injections of ipecacuanha highly in *choleriform diarrhœa* of children, and in *tuberculous diarrhœa*, and Polichronic not only corroborates him, but also affirms that the same treatment is of great value in *colliquative sweats*. In a very valuable clinical paper (*Atlanta Med. and Surg. Journ.*, 1875) Dr. A. A. Woodhull brings forward very strong evidence of the value of the remedy not only in dysentery but also in choleriform diarrhœas. The drug appears to exert a direct influence upon the hepatic and intestinal glands, and may be tried with great hope of success wherever there is decided glandular derangement.

In *catarrhal jaundice*, and in *intermittents* or *remittents* accompanied by congestion of the portal circulation, ipecacuanha is often very serviceable.

As a *hæmostatic*, ipecacuanha has been recommended by Trousseau, and Pecholier asserts that in *hæmoptysis* it is a specific (*Bull. Thérap.*, xcvii. 49).* It has been given, with asserted advantage, in *flooding* after child-birth, and Dr. Carrigen claims for it *oxytocic* powers (*N. Y. Med. Journ.*, 491, 1878).

ADMINISTRATION.—As an emetic, ipecacuanha is generally administered in powder, thirty grains being given every fifteen or twenty minutes until the desired effect is produced. For a child a year old the emetic dose is five grains. Its action should be aided and hastened by large draughts of lukewarm water. As a nauseant the dose is from two to five grains. In dysentery it is generally best to begin with a full emetic dose, or with ten grains repeated every half-hour until emesis is produced. Two or three hours after vomiting, fifteen drops of laudanum should be exhibited, followed in twenty minutes by five to ten grains of ipecacuanha in *pill-form;* this should be repeated every two or three hours, the amount of the opium being lessened and that of the ipecacuanha increased, according to circumstances. The object is to have as much of the ipecacuanha retained as possible. Another plan is to give larger doses (twenty grains), repeated every two, four, or six hours, mustard being applied to the epigastrium and opium exhibited as before; and it is said that after two or three doses tolerance is established and the drug retained. In India, enemata of ipecacuanha are often employed, either as a substitute for or an adjuvant to its use by the mouth. This treatment has recently been imitated by Chouppe and others, and has been practiced quite extensively in my ward in the Philadelphia Hospital. It is undoubtedly frequently efficient in abdominal complaints, and the gastric symptoms are almost always avoided. In chronic cases the repetition of the enemata sometimes produces so much local irritation as to forbid their continuance. I have been accustomed to give a scruple of the powder with starch and laudanum, repeated every four hours. A decoction of the drug is to be preferred, as probably causing less local irritation and being more thoroughly absorbed. To an adult, Chouppe gives two injections of a decoction daily, each lavement representing two and a half drachms of the drug.

As a counter-irritant, ipecacuanha is rarely used in this country; but in England a liniment is employed composed of four parts of the powder to fourteen parts of olive oil.

The preparations for internal use are: a *syrup* (*Syrupus Ipecacuanhæ*, U. S.,—Fld. ext. 5 to 100),—dose, as an emetic for an infant, one to two teaspoonfuls; a *wine* (*Vinum Ipecacuanhæ*, U. S.,—Fld. ext. 1 to White

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* Consult *Pacific Surgical and Med. Journ.*, 1876.

Wine 7),—dose, the same as the syrup; and a *fluid extract* (*Extractum Ipecacuanhæ Fluidum*, U. S.), dose, as an emetic, for an adult thirty drops. *Trochisci Ipecacuanhæ*, U. S., *Trochisci Morphinæ Ipecacuanhæ* U. S., are used in catarrh of the throat as a local application.

Emetia is not officinal, but has been used by Dr. Dyce Duckworth (*London Pharmaceutical Journal*, March, 1872) and his colleagues in doses of from one-twelfth to one-sixth of a grain.

SANGUINARIA—BLOODROOT. U.S.

This is the rhizome of an indigenous perennial herb, Sanguinaria Canadensis. It occurs in pieces two or three inches long, reddish brown externally, a bright somewhat orange red internally, and, when fresh, full of a similarly-colored juice. It contains two asserted alkaloids, *Puccin* and *Porphyroxin*, besides an alkaloid, first discovered in it by Dr. Dana in 1829, and named by him *Sanguinarina*, but which is identical with the alkaloid of Chelidonium majus—*Chelerythrin*. As the latter was not discovered by Probst until 1839, it is obvious that the name sanguinarina has the priority and should be adopted. *Sanguinarina* occurs in colorless stars or groups of fine needle-like crystals, tasteless when dry, of a sharp burning taste when moistened with alcohol, very irritating to the nasal mucous membrane, and uniting with acids to form brilliant red, mostly soluble, salts.

Physiological Action.—In full doses sanguinaria acts upon man as a harsh emetic, and in overdoses, according to Dr. Tully, it produces, with the vomiting, burning at the stomach, faintness, vertigo, diminished vision, general insensibility, coldness, extreme reduction of the force and frequency of the pulse, together with great irregularity of action and often palpitation of the heart, great prostration of muscular strength, and sometimes a convulsive rigidity of the limbs. Fatal poisoning of several persons occurred by it at Bellevue Hospital; but the only symptoms recorded are "racking, burning pains, and tormenting thirst."

The only physiological study of the drug as yet made is that of Dr. Robert Meade Smith (*Amer. Journ. Med. Sci.*, Oct. 1876). He finds that it causes in mammals vomiting, purging, profuse salivation, followed by collapse, dilated pupils, with sometimes clonic convulsions, and death from asphyxia. As the result of numerous experiments, he concludes that the convulsions are spinal, but associated with decrease reflex excitability, which is at first due to an excitation of Setschenow's centre, but afterwards to a depression of the spinal centres; and that there is a progressive lowering of the pulse and arterial pressure after large doses, caused partly by a direct action upon the heart, partly by paresis of the vaso-motor centres. Moderate doses of sanguinarina Dr. Smith finds to at first irritate the vaso-motor centres, and so produce a primary rise of the arterial centre. Muscular contractility is reduced by it, salivation greatly increased, and the respiration progressively rendered slower and shallower by a direct action upon the centre.

Therapeutics.—As an emetic, sanguinaria has fallen into well-deserved disuse. Indeed, I have never known of its employment except as a stimulant expectorant in obstinate *bronchitis*, and even then with doubtful advantage.

Administration.—The crude drug is very rarely used; the emetic dose of the powder is from ten to sixty grains. Prof. R. P. Thomas, in experiments upon himself and others with the alkaloid, found that in a dose of from one-eighth to one-twelfth of a grain it acted as an expectorant, without disturbing the stomach; one-sixth or one-fourth of a grain, given every two or three hours, generally nauseated, the emetic dose being half a grain repeated every ten minutes. One-sixth of a grain every three hours, in the course of two or three days, reduced the pulse from five to twenty-five beats per minute. The expectorant dose of the *tincture* (*Tinctura Sanguinariæ*, —1 to 6.6, U. S.) is gtt. xx to xl; of the *vinegar* (*Acetum Sanguinariæ*, U. S.), fifteen to thirty minims; of the *fluid extract* (*Extractum Sanguinariæ Fluidum*, U. S.), three to five minims.

APOMORPHINÆ HYDROCHLORAS—HYDROCHLORATE OF APOMORPHINE. U.S.

Apomorphine was discovered by Dr. Matthieson and C. R. A. Wright (*Proceedings Roy. Soc.*, xvii. 455), who made it by the action of a strong solution of hydrochloric acid upon morphine. A probably better method of preparation is that of E. L. Mayer (*Berichte Deutsch. Chem. Gesell.*, Berlin, 1871, iv. 121), in which the morphia is treated with a solution of the chloride of zinc at 120° C. Apomorphia occurs as a snow-white powder, which is permanent when dry, but when moist soon becomes green. Its solution suffers this change, which is probably an oxidation, in a few minutes by heat (Matthieson and Wright), and in a few hours at ordinary temperature; and in the course of some weeks the green tint deepens into a black. Bichromate of potassium turns it a dense yellow orange; bichromate of potassium and concentrated sulphuric acid make a dark red with it; and with neutral chloride of iron it strikes an amethyst color. It differs from morphia in being soluble in cold water. The officinal salt is soluble in six parts of water.

Physiological Action.—In doses of from one to five milligrammes in frogs apomorphia causes at first a stage of restlessness, which, after a time, yields to an increasing sluggishness and muscular weakness that may end in real or apparent death. In some instances there are violent convulsions, both clonic and tonic in character.* Sometimes after both respiration and cardiac action have apparently ceased, recovery occurs.

When small doses (1 to 2. milligrms.) of the alkaloid are given to dogs, vomiting, without any other decided symptoms, is induced; after slightly larger amounts, the vomiting is severe, and accompanied by free salivation and muscular tremblings. After very large doses, vomiting does not occur, but a condition of intense restlessness is soon developed, the animal often jumping in the air, running about the room, howling and champing constantly. The slightest noise or alarm throws him into violent excitement and terror; with pupils dilated, ears drawn stiffly back, he endeavors to get out of the apartment, and even to climb the wall. After still larger amounts (4 or 5 gr.), to this excitement is soon added failing muscular strength, and the hind legs are dragged behind the animal in his movements. The respiration is exceedingly hurried, and convulsions are suddenly developed. The paresis and convulsions increase, so that the animal lies upon his back, kicking wildly into the air, and finally he dies asphyxiated. Rabbits cannot vomit, but the general symptoms produced by the alkaloid in them and in cats are exactly parallel with those just described as occurring in the dog. Very small doses (10 milligrms., Harnack) suffice to kill the rabbit. On chickens and pigeons, according to C. David (*Gaz. Méd.*, 1874, p. 465), it acts very much as it does upon dogs; the stage of excitement is very marked. After death no distinctive lesions are to be found, unless, as Quehl (*loc. cit.*, p. 19) believes, there is habitually an excessive hyperæmia of the pons varolii.

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* Consult E. Harnack, *Arch. Exper. Pathol. und Pharm.*, ii. 291; Max Quehl, *Ueber der Physiol. Wirk. des Apomorphins*, Inaug. Diss., Halle, 1872; I. B. V. Bourgeois, *Del Apomorphine*, Paris, 1872; E. Reichert, *Phila. Med. Times*, x. 110; G. Valentin, *Arch. Exper. Path. u. Pharm.*, xi. 399.

To the therapeutist the chief interest in apomorphia is in connection with its power of producing vomiting; but before taking this up I shall endeavor to portray what is known in regard to the physiological actions of the drug.

Nervous System.—The action of apomorphia upon the cerebrum seems to be that of a primary stimulant delirifacient, and final paralyzant. The cause of the convulsions at present cannot be considered as made out.* According to Reichert's experiments both the sensory and motor nerves are first stimulated and afterwards paralyzed. In opposition to the experiments of Quehl, Harnack found that the muscles in the frog around the place of injection soon lost their irritability, evidently from the poison reaching them in a concentrated form by imbibition. He also separated one hind leg of a frog from the rest of the body, leaving only the nerve intact, and then poisoned with apomorphia. After voluntary motion had ceased, the muscles of the intact leg were far less excitable than were those of the leg to which access of the poison had been prevented. These experiments have been confirmed by Reichert, and there can be no doubt that apomorphia is a muscle-poison.

Circulation.—The reports upon the action of this drug upon the circulation are somewhat discordant. Seibert (*London Med. Record*, i. 44), Max Quehl, and Bourgeois affirm that the blood-pressure is not affected even by toxic doses. Harnack, however, found, after large doses in dogs, a distinct fall of arterial pressure, and also that apomorphia is a direct paralyzant of the cut-out frog's heart. The latter fact has been confirmed by Reichert, who has also shown that the mammalian heart is similarly affected by the drug; and that finally this cardiac action causes a fall of the arterial pressure. Preceding the fall there was in Dr. Reichert's experiments a distinct rise of arterial pressure, which was prevented by previous section of the cord, and was therefore probably due to stimulation of the vaso-motor centres. Therapeutic doses of the drug have no distinct action upon the force of the circulation. The pulse-rate is markedly increased by small and large doses of apomorphia, the maximum usually being reached about the time vomiting is fairly established; subsequently, in poisoning, the pulse falls below normal. Reichert believes the rise to be due to stimulation of the accelerators, and the fall to the influence upon the heart-muscle.

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* The only one who has carefully studied them is Reichert, and his published account is self-contradictory. He reasons that the convulsions are chiefly spinal, and yet says (p. 111) that in mammals, after section of the spinal cord, except "in very exceptional cases," they are confined to the anterior part of the body.

Respiration.—Usually the respiration-rate is increased by decided or toxic doses; although the amount of increase varies greatly, it is often very large. Harnack says that after toxic doses the rate rises very much before the occurrence of convulsions, but Reichert has not been able to observe this. During the convulsive period the respirations become irregular and unequal, and they finally grow more and more shallow and infrequent, until death results from a paralysis of the respiratory centres. Both Harnack and Reichert have noted that in the rabbit previous section of the par vagum does not prevent, but rather increases this acceleration, so that it would seem that apomorphia stimulates the respiratory centres; but Reichert affirms that in the cat and dog no increase of the respiration-rate occurs under the action of the drug if the pneumogastrics have been cut.

Temperature.—The action of apomorphia upon the temperature appears to be very trifling and inconstant. According to Ziolkowski (*Apomorphin*, Inaug. Diss., Griefswald, 1872), the bodily heat usually falls after large doses from 0.1° to 0.5° C. Moerz noticed in one man that the temperature rose during the vomiting two-tenths of a degree; whilst Bourgeois affirms that in man the drug has no influence over the temperature, and Reichert has seen in animals a rise follow the hypodermic, but not the intravenous injection of the alkaloid.

Emesis.—Dr. Gee (*St. Bartholomew's Hosp. Rep.*, vol. v. p. 215) was the first to announce that apomorphia is a certain and prompt emetic, producing but little nausea, and having the great advantage of acting in very small dose, a tenth of a grain being sufficient, when injected under the skin, to cause vomiting in ten minutes. His statements have been confirmed by very many observers, excepting that the dose employed by Gee is usually considered too large. Thus, Dr. Pierce (*British Medical Journal*, 1870, p. 274) employs one-fifteenth of a grain, and M. Bertrand (*Gaz. Méd.*, 1874) has vomited with .06 grain. The time required for action depends largely upon the amount of the drug exhibited. After very small doses twenty minutes may elapse, and in Bourgeois's experiments 0.45 grain produced violent vomiting in less than two minutes. After these large doses the emesis usually recurs once or twice at intervals of a quarter to half an hour.* The vomiting seems to be of centric origin, as Reichert has succeeded in producing it when the thoracic aorta was tied so as to prevent any of the poison reaching the stomach.

A knowledge of the effects of narcotics upon the action of apomorphia is, of course, of great practical importance. There is as yet very little clinical evidence. A case of poisoning with bitter almonds has indeed been reported (*Schmidt's Jahrbücher*, Bd. clv. p. 272), in which the injection of 0.013 grain of the alkaloid was followed by prompt emesis; but it is evident that no inference in regard to narcotic poisoning could be drawn from this. It is inconceivable that there should be any differences in the relation between apomorphia and narcotism in man and in animals, and the subject has been investigated, with mostly similar but insufficient results, upon animals by several observers.† In dogs chloral retards, or, if in sufficient dose, prevents, the emesis of apomorphia; during chloroform-sleep the alkaloid is affirmed by David and Dujardin-Beaumetz to be powerless; but MM. Coyne and Budin state that it will produce emesis even during profound anæsthesia if the dose be large enough; David found that in a dog three centigrammes of morphia prevented the occurrence of the vomiting. It is plain that these experiments prove no more than that narcotics influence the action of apomorphia as they do that of every other emetic; and the probabilities seem to be that the alkaloid produces vomiting more surely than do our ordinarily used drugs. The emesis is probably the result of a stimulant action exerted upon the nerve-centres; and the fact that after toxic doses vomiting does not occur indicates that in such amounts the drug paralyzes these centres.

Local Action.—Apomorphia is not an irritant, so that the hypodermic use of even concentrated solutions of it elicits in the lower animals no evidences of pain. In man the injections have sometimes caused intense pain, probably because they had been originally improperly prepared or had undergone chemical change.

THERAPEUTICS.—There is now sufficient evidence to show that apomorphia is a safe and reliable emetic, possessed of advantages which have already been sufficiently dwelt upon. It may be used whenever it is desired simply to empty the stomach. In *narcotic poisoning* there is no reason why it should not be given hypodermically whilst sulphate of zinc or some mechanical emetic is exhibited by the mouth. As an *expectorant*‡ apomorphia is employed with asserted great advantage in the *suffocative catarrh* of infants, when an emetic is required to get rid of the bronchial exudation. Under these circumstances it is said not only to act efficiently as an emetic, but also in rendering the mucus more copious and fluid. It is claimed that in the early stage of *acute bronchitis* it rapidly causes copious, loose secretion, and that in *chronic bronchitis* it is very useful when expectoration is scanty.

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* For the doses required to vomit various animals, see *Gaz. Méd.*, 1874, p. 466.

† E. Harnack (*loc. cit.*); O. C. David (*Gaz. Méd.*, 1874, p. 465); Dujardin-Beaumetz (*Bull. Thérap.*, Oct. 1874).

‡ Dr. Jurasz (*Centralb. f. d. Med. Wiss.*, 1874, 499); Dr. M. Wertner (*Wien. Med. Presse*, 1876, 269); Dr. Carl Beck (*Deuts. Med. Wochen.*, 1881, 156).

Administration.—As an emetic, apomorphia has usually been administered hypodermically, in doses of one-tenth of a grain, repeated every ten minutes until some effect is induced; but it may be exhibited by the stomach in double the amount. In cases of severe poisoning, where time is of great moment, it may be well to give as much as one-fourth of a grain at a single injection. In feeble persons, however, caution must always be exercised in using it, as one-fifteenth of a grain has caused death in seven minutes in an adult, fifty-four years old, suffering from chronic bronchitis with marked emphysema (*Med. Rec.*, 1877, 664). Wertner gives the expectorant dose as 0.07 to 0.15 for children, or double the amount for the adult, repeated every two hours by the mouth. Care must be exercised in its use in children. In Vulpian's clinic the dose is from 0.07 to 0.09 grain. Dr. Loeb (*Schmidt's Jahrb.*, Bd. clv. p. 272) gave hypodermically 0.03 grain to an infant thirteen months old suffering from capillary bronchitis; the free vomiting which was induced left the infant much exhausted. In a very few cases apomorphia has failed to vomit, and even caused startling symptoms: so that care should be exercised not to push the remedy too far. M. Carville affirms that three-tenths of a grain has caused a syncopal condition in an adult, and M. Prevost details a case (*London Medical Record*, 1875, p. 183) in which syncope and threatening collapse were apparently induced by a very small dose. In children especially must care be exercised, since, according to Harnack, the drug is very liable to produce collapse. The ordinary solutions of apomorphia undergo a rapid change, becoming green; and Dr. Loeb has reported a case in which very alarming symptoms followed the use of such a solution. M. Constantine Paul states that if glycerine be used as the sole menstruum the solution will keep three or four days. M. Carville (*Gaz. Hebdom.*, 1874, p. 408) affirms that glucose acts well as a preservative, and it is claimed that a few drops of muriatic acid will suffice for the same purpose.

A very useful stimulating emetic is *mustard flour*, very prompt and even violent in its action. It acts as a mechanical emetic, and is to be used when it is desired simply to evacuate the stomach rapidly, and especially when there is torpor of the viscus. As it is generally to be had at once, it is especially useful in such emergencies as *narcotic poisoning*. It has also been commended in *nervous collapse*, such as is seen in *malarial pernicious chill*. The dose is a heaped dessertspoonful in half a pint of water, repeated, if necessary, in ten minutes. As mustard is irritant to the stomach, if it fail to act it should not be repeated more than three or four times, even in narcotic poisoning.

Squill (*Scilla*) is sometimes used as a harsh, stimulating mechanical emetic.

MINERAL EMETICS.

The mineral emetics in ordinary use are tartar emetic, sulphate of zinc, and sulphate of copper. As they are all considered elsewhere, it is only necessary here to say a few words in regard to their use as emetics.

Tartar emetic is the most depressing of all the substances here spoken of as emetics. It is rather slow in its action, but the vomiting which it causes is preceded and accompanied by intense nausea, and is exceedingly violent and persistent. For these reasons, tartar emetic is rarely used simply to unload the stomach, except in the absence of more eligible substances. Its use in inflammatory diseases is discussed elsewhere. It is usually believed to be a centric emetic acting by absorption.

Sulphate of zinc is an excellent and prompt mechanical emetic, producing little or no irritation, and is to be preferred above all others when an emetic of such nature is needed. In *narcotic poisoning* it should be given in combination with ipecacuanha, and perhaps be preceded by mustard whilst it is being obtained from the apothecary. Thirty grains of it with fifty of ipecacuanha may be given as the first dose, and a mixture of fifteen grains of the former to thirty grains of the latter be administered every fifteen minutes until the desired effect is produced or one hundred grains of the zinc are taken. Beyond the latter amount it would be hardly safe to go, for fear of causing gastro-enteritis.

Sulphate of copper resembles the corresponding zinc salt as an emetic, but is more severe and irritating, and more capable of causing gastro-enteritis. The full dose in narcotic poisoning is from five to ten grains, which should not be repeated more than once.

Powdered *alum* is a mechanical emetic, which has been especially recommended in *membranous croup*, on account of its being believed to act beneficially upon the diseased surfaces in its passage up and down the throat. A heaped teaspoonful of it may be given in molasses or syrup. In my experience alum has proved an unreliable emetic.

CLASS II.—CATHARTICS.

Purgatives, or cathartics, are those drugs which are employed in medicine to act upon the intestinal tract so as to produce purgation, or catharsis. The question has recently been a good deal discussed as to whether purgation is produced by an increase of the watery secretions or of the peristaltic movements of the intestines.

M. Thiry (*Sitzungsberichte der k. k. Acad. d. Wissensch.*, Bd. l.) experimented upon this subject by drawing out a knuckle of intestine through a wound in the linea alba, cutting it free from the remainder of the gut without injuring its nerves or blood-vessels, sewing together the distal and proximal ends of the main portions of the intestines so as to re-form a continuous tube, and then, after closing up one end of the knuckle, forcing the other into the wound so as to make an intestinal *cul de sac* which could be studied through a fistulous opening. In dogs which had recovered after this operation, Thiry found that large doses of the sulphate of magnesium, of senna, or of croton oil failed alike to increase the secretion of the separated piece of intestine, although they induced violent purging; further, neither concentrated solutions of Epsom salt, nor infusion of senna, even though kept in the *cul de sac* for some time, were able to increase its secretion by exosmose. More recently, Dr. S. Radziejewski has made an elaborate investigation of the subject (*Reichert's Archiv für Anat.*, 1870, p. 37). As the result of a number of very careful analyses, he asserts that there is nothing to be found in the stools produced by the sulphate of magnesium, by calomel, castor oil, croton oil, senna, or gamboge, to indicate that they are anything besides the ordinary contents of the upper and lower bowels. Dr. Radziejewski confirms the fact observed by C. Schmidt, that the stools of purgatives contain a great deal of soda, but denies that this proves at all that they are transudations, asserting that the alkaline salts are derived simply from the pancreatic fluid. Dr. Radziejewski also corroborates the confirmation by Asp (*Ludwig's Arbeiten*, 1868) of the discovery of Moreau,* that division of the intestinal nerves is followed by free serous exudation into the gut, but denies that purgatives act by paralyzing the vaso-motor nerves, because croton oil injected into a loop of intestine which had been separated by two ligatures from the remainder of the gut caused both vomiting and purging. As no emulsifying substance was contained in the intestine, he declares that no absorption could have occurred, and that consequently the general intestinal disturbance was simply due to increased peristaltic action, caused by the internal local irritation of the oil propagated along the intestines. The experiments of Thiry have also been repeated by Radziejewski with croton oil and with sulphate of magnesium, as well as by Schiff (*Nuove Richerche sul Potere digerente*, H. Morgagni, 1867) with aloes, jalap, and sulphate of sodium. In all cases the results were the same as those already noted as obtained by Thiry. Carrying his investigations still further, Radziejewski, by forming intestinal fistulæ at such positions as would enable him to study the rate of passage of the intestinal contents, found that after a dog is fed upon flesh the small intestine empties the partially-digested food into the colon so rapidly and in such quantity as to constitute, so to speak, a normal diarrhœa, and that the long delay in the exit and the hardening of the fæces occur in the large intestine. The liquid which passed into the ascending colon agreed in all its characteristics with the stools of purgation. Dr. Radziejewski also claims to have established by direct experimentation that the peristaltic movements of the small intestine were affected very decidedly by drastics, and to some degree by Epsom salt, and that in all cases the large intestine was still more intensely acted upon. Although these experiments are very interesting, it cannot be allowed that they prove what is claimed for them, namely, that purgatives cause no increase of intestinal secretion, but only of peristaltic action. So much violence to natural conditions is done in the experiments after the method of Thiry that they seem worthy of very little weight. The assumption of Radziejewski, that croton oil confined in a loop of intestine is not absorbed, is a pure assumption, and his experiment does not warrant the conclusions drawn from it.

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* *Comptes-Rendus*, t. lxvi., 1868; also Asp, *Ludwig's Arbeiten*, 1868.

The other facts brought forward seem to prove only that increased peristalsis, especially of the large bowel, plays a more important rôle in the induction of diarrhæa than has been assigned to it.

Leaving out of sight for the moment all clinical evidence, the fact that previous section of the par vagum prevents the action of purgatives* is opposed to the German theory, since it is almost certain that the division of the nerves of the neck does not arrest peristaltic movements. Further, Armand Moreau (*Archives Gén.*, 6e sér., t. xvi. p. 234) has found that a solution of Epsom salt placed in a knuckle of intestine isolated by means of two ligatures does cause a serous exudation into it, and in repeating M. Thiry's experiments (*Gaz. Méd.*, 1871) he has obtained opposite results. His experiments indicate three possible sources of fallacy in the work of the previous investigators: first, if the Epsom salt be not kept in the intestine for a sufficient length of time (some hours), no transudation occurs; second, in some cases the inner end of the isolated piece of intestine fails to adhere, so that the opening is not obliterated, and the matters injected into the arrested *cul de sac* really pass into the peritoneal cavity; third, atrophy of the mucous membrane and glandular apparatus of the *cul de sac* often follows almost at once upon the operation, and of course necessitates a negative result in the subsequent experiments. Recently, Dr. Lauder Brunton, in a communication to the Medical Society of London, has stated that he had repeated Moreau's experiments, and found that sulphate of magnesium injected into the intestine of a cat caused about two-thirds of a drachm of fluid to be secreted in four hours by each inch of the bowel operated on, although the proportion of sulphate was only one grain to an inch (*Med. Press and Circular*, Dec. 31, 1873). In further experiments by Dr. Brunton, gamboge, elaterium, and croton oil gave results similar to those of the Epsom salt (*Practitioner*, May, 1875). M. Vulpian has repeated the experiments of Moreau, and found that both sulphate of magnesium and jalap provoke a "true intestinal catarrh;" the vegetable cathartic at the same time increasing the peristaltic action, but the saline having no such effect (*Gaz. Méd.*, 1873, p. 300). M. Legros (*Ibid.*), and also M. Van Braam Houckgeest (*Pflüger's Archiv*, 1872, 266), have experimentally determined that salines do not increase the activity of the peristaltic movements.*

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* See paper by the author, *American Journal of the Medical Sciences*, vol. lx., 1870.

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* Dr. Matthew Hay (*Journ. Anat. Physiolog.*, xvi., xvii.) has most exhaustively investigated the action of saline cathartics. Space is wanting in which to discuss his article in detail, but the following are his results as formulated by himself:

1. A saline purgative always excites more or less secretion from the alimentary canal, depending on the amount of the salt and the strength of its solution, and varying with the nature of the salt.

2. The excito-secretory action of the salt is probably due to the bitterness as well as to the irritant and specific properties of the salt, and not to osmosis.

3. The low diffusibility of the salt impedes the absorption of the secreted fluid.

4. Between stimulated secretion on the one hand, and impeded absorption on the other, there is an accumulation of fluid in the canal.

5. The accumulated fluid, partly from ordinary dynamical laws, partly from a gentle stimulation of the peristaltic movements excited by distention, reaches the rectum and produces purgation.

6. Purgation will not ensue if water be withheld from the diet for one or two days previous to the administration of the salt in a concentrated form.

7. The absence of purgation is not due to the want of water in the alimentary canal, but to its deficiency in the blood.

8. Under ordinary conditions, with an unrestricted supply of water, the maximal amount of fluid accumulated within the canal corresponds very nearly to the quantity of water required to form a 5 or 6 per cent. solution of the amount of salt administered.

9. If, therefore, a solution of this strength be given, it does not increase in bulk.

10. If a solution of greater strength be administered, it rapidly increases in volume until the maximum is attained. This it accomplishes in the case of a 20 per cent. solution in from one to one and a half hours.

11. After the maximum has been reached, the fluid begins gradually and slowly to diminish in quantity.

12. *Cæteris paribus*, the weaker, or in other words, the more voluminous the solution of

The experimental evidence bearing upon the question under discussion is, so far as I know, all included in the above summary: it is very far from dem-

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the salt administered is, the more quickly is the maximum within the canal reached; and accordingly purgation follows with greater rapidity.

13. Unless the solution of the salt is more concentrated than 10 per cent. it excites little or no secretion in the stomach.

14. The salt is absorbed with extreme slowness by the stomach of the cat.

15. The salt excites an active secretion in the intestines, and probably for the most part in the small intestine, all portions of this viscus being capable of yielding the secretion in almost equal quantities.

16. The bile and pancreatic juice participate but very little in the secretion.

17. The secretion is probably a true *succus entericus*, resembling the secretion obtained by Moreau after division of the mesenteric nerves.

18. The secretion is promoted by local irritation of the intestine, as by ligatures, but only in the immediate vicinity of the irritation.

19. Absorption by the intestine generally is reflexly stimulated by such irritation (the effect of numerous ligatures applied at points remote from the seat of the injected salt being to diminish the amount of purgative fluid by accelerated absorption).

20. If the salt solution be injected directly into the small intestine, the stronger within certain limits the solution is, the greater will be the accumulation of fluid within the intestine.

21. This difference is not observed when the salt is administered *per os*, as the strong solution becomes diluted in the stomach and duodenum before passing into the intestine generally.

22. The difference is due to the local action of the salt on the mucous membrane, and probably more to an impeded absorption than to a stimulated secretion.

23. When the salt is administered in the usual manner, it appears, in the case of the sulphate of magnesia and sulphate of soda, to become split up in the small intestine, the acid being more rapidly absorbed than the base.

24. A portion of the absorbed acid shortly afterwards returns to the intestines.

25. After the maximum of excretion of the acid has been reached, the salt begins very slowly and gradually to disappear by absorption, which is checked only by the occurrence of purgation.

26. During the alternations of absorption and secretion of the acid, it is the salt left within the intestine which excites secretion, the absorbed and excreted acid exerting no such action whilst in the blood, or during the process of its excretion, as Headland believed.

27. The salt does not purge when injected into the blood, and excites no intestinal secretion.

28. Nor does it purge, when injected subcutaneously, unless in virtue of its causing local irritation of the abdominal subcutaneous tissue, which acts reflexly on the intestines, dilating their blood-vessels, and perhaps stimulating their muscular movements.

29. The sulphate of soda exhibits no poisonous action when injected into the circulation.

30. The sulphate of magnesia is, on the other hand, powerfully toxic when so injected, paralyzing first the respiration and afterwards the heart, and abolishing sensation or paralyzing the sensory-motor reflex centres.

31. Both salts, when administered in the usual manner, produce a gradual but well-marked increase in the tension of the pulse.

32. According as the salt-solution within the intestine increases in amount, there occurs a corresponding diminution of the fluids of the blood.

33. The blood recoups itself in a short time by absorbing from the tissues a nearly equal quantity of their fluids.

34. The salt, after some hours, causes diuresis, and with it a second concentration of the blood, which continues so long as the diuresis is active.

35. As the intestinal secretion excited by the salt contains a very small proportion of

onstrating that increased peristalsis, and not increased secretion, is the cause of the watery stools produced by purgatives. The evidence, both experimental and clinical, is indeed overwhelmingly in favor of increased secretion. The facts proven by clinical observations and by experiment—that purgatives increase greatly the secretion in an isolated knuckle of intestine, that various purgatives act when taken into the blood, and that in these cases elimination by the bowels occurs; that at least some purgatives (Headland, *Action of Medicines*, London, 1867, p. 443), when given by the mouth, are absorbed, disappearing from the alimentary canal and reappearing when purgation occurs; that the stools induced by overdoses of various drastics, as elaterium, are so enormous as to cause the profoundest depression, and even choleraic collapse, in a very few hours; that the discharge of hydragogues contains a very large percentage of soda, the alkali of the serum; that the relief obtained in portal congestion by the depletion of salines is very marked—are, when viewed together, to my mind, incompatible with any other belief than that purgatives cause increased secretion, as well as, in many cases, increased peristalsis, in the alimentary canal.

The question of the action of drugs upon the flow of bile is a very important one, the evidence concerning which is best considered under two headings: first, the experimental; second, the clinical.

The experiments upon this subject which have attracted most attention are those of Dr. Scott, and of the Edinburgh committee, of which Prof. Bennett was chairman and Drs. Rutherford and Gamgee the workers. The method employed both by Dr. Scott and by the Edinburgh committee was to make biliary fistulæ in dogs in the usual physiological method, and, after recovery from the operation had taken place and the bile regularly escaped by the external orifice, to administer the drugs, especially calomel and podophyllin, and study the effects upon the excretion of bile. Of the accuracy of their experiments I do not think there can be any reasonable doubt. I believe they prove that in dogs with biliary fistulæ mercury has no effect upon the flow of bile unless given in such quantities as to deteriorate the general health, when it diminishes the biliary secretion. The result does not, however, warrant the further conclusion that mercury does not increase the flow of bile in healthy dogs. The animals were in such an unnatural condition that, in spite of the daily ingestion of much more than the normal amount of food, they progressively emaciated, and finally died apparently of inanition:

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organic matter as compared with the inorganic matter, the purgative removes more of the latter than the former from the blood. In certain cases a large quantity of the salts of the blood is thus evacuated.

36. The amount of the normal constituents of the urine is not affected by the salt.

37. After the administration of sulphate of magnesia much more of the acid than of the base is excreted in the urine.

38. The salt has no specific action in lowering the internal temperature of the body, or has it only to a very small extent.

39. It reduces, however, the absolute amount of heat in the body.

moreover, the innervation, and very possibly the blood-supply, also, of the liver was very much interfered with. Under these circumstances it is clearly conceivable that the mercurial or other purgative might in the uninjured dog affect the biliary secretion, and yet fail to do so in the experiment, hindered by some obscure yet efficient cause. Very recently, Dr. A. Röhrig has experimented (*Stricker's Medicin. Jahrbücher*, 1873) in a method which simulates more closely the natural conditions; although even the results thus obtained do not seem to me conclusive. In curarized dogs in which life was maintained by artificial respiration, he placed a glass tube in the gall-duct so that the bile could escape only through it. Under these circumstances, of course, after a time secretion ceased; and Dr. Röhrig experimented not only on the effect of remedies upon the secretion whilst naturally going on, but also upon their power of re-establishing it. He found that large doses of croton oil (eighteen drops) thrown into the duodenum caused an immediate very great increase, or a re-establishment, of the secretion. After the oil, the vegetable cathartics were most active, decreasing in power in the following order: colocynth, jalap and aloes, rhubarb and senna. Castor oil had very little influence, as had also the bitter salts. Calomel, even in large doses (twenty grains), very rarely re-established the secretion, but its power of increasing and maintaining it beyond the natural time for cessation was very marked.

Prof. W. Rutherford, in a most extended and laborious research, used the method of Röhrig with some improvements (*Trans. Roy. Soc. Edinb.*, xxix.). The drug, mixed with bile to facilitate absorption, was injected directly into the duodenum by means of a hypodermic syringe. The results obtained may be briefly summarized as follows:

Croton Oil in enormous doses neither purged nor affected the biliary secretion.

Podophyllin very greatly increased biliary secretion, especially when in such small doses that it did not purge severely.

Aloes very greatly increased biliary secretion, the doses used not purging greatly.

Rhubarb, *Colchicum*, *Iridin*, *Colocynth*, *Jalap*, *Sulphate of Sodium*, *Phosphate of Sodium*, *Rochelle Salt*, very greatly increased biliary secretion, at the same time purging.

Senna, *Taraxacum*, *Scammony*, *Gamboge*, *Castor Oil*, *Sulphate of Magnesium*, *Chloride of Ammonium*, acted very feebly, if at all, upon the liver.

Leptandrin, *Chloride of Sodium*, *Bicarbonate of Potassium*, had some, but not a powerful, effect on the liver.

Euonymin, *Sanguinarina*, *Ipecacuanha*, had very powerful influence on the secreting of bile, and did not purge.

Calomel had no effect on the biliary secretion, but when to it a minute proportion of corrosive sublimate was added the effect was very marked; *Corrosive Sublimate* acted as a very powerful biliary stimulant.

There is one objection to the experiments of Rutherford and Vignal, entirely independent of the method employed,—there were rarely more than two experiments with any one substance, and in several instances two experiments gave antagonistic results. It is very possible, indeed probable, that if a number of experiments had been made with each drug, the variation in results would have been much greater.

What is to be drawn from these various facts? Evidently, I think, but one conclusion,—that the experimental evidence at present does not warrant positive deductions as to the effect of purgatives upon the biliary secretion of healthy dogs. The canine diet and digestion are so different from the human that it is to be expected that medicines acting upon the digestive apparatus will influence dogs differently from man: thus, I have given doses of elaterium that would have killed a man to some of the carnivora without causing the slightest purging. In view of these facts, the only fairly deducible conclusion in regard to the experimental evidence that has been brought forward is, that it must be received with the greatest reserve or be entirely laid aside when we desire to study the question as to the cholagogue action of remedies upon man, and that our conclusions are most safely based upon clinical evidence.

In regard to the drastics, there can be little doubt that almost any irritant purgative will to a greater or less extent increase the escape of bile, probably both by increasing its flow into the duodenum and by sweeping it out of the small intestine before absorption can take place. There are, however, two actively purgative substances for which it is especially claimed that they are cholagogues: namely, calomel and podophyllin. The discussion of the action of these will be found under their respective headings.

Dr. Hugo Heinrichsen has found (*Schmidt's Jahrb.*, Bd. ccii. p. 214) that the excretion of urine is diminished by purgatives; very much so by Glauber and Epsom salts; slightly by castor oil and compound liquorice powder. The solids of the urine are not sensibly affected by the vegetable cathartics. Under the influence of the salines the solids of the urine are increased. Glauber salts is said to be partially converted into an alkaline carbonate, and to thereby give an alkaline reaction to the urine.

Various divisions of purgative medicines have been proposed by different authors; but probably the most convenient arrangement is as follows:

1. *Laxatives.*—Medicines which simply unload the bowels, and are not able to cause active purgation, even when given in very large doses.

2. *Purges.*—Medicines which purge actively, but are not capable of acting as poisons, even in very large amount.

3. *Hydragogues*, which produce very large watery stools without much irritation. In overdoses, medicines of this class assume some of the characters of those of the next.

4. *Drastics*, which cause great irritation of the alimentary mucous membrane, and in overdoses are violent poisons.

It must be borne in mind that this classification is somewhat artificial;

that the effects of the remedies depend much upon the doses in which they are administered, so that in sufficiently minute quantity a drastic may act as a laxative; and that the dividing-lines between the groups are not very distinct.

Enemata.—When it is desired simply to unload the lower bowels, the object can often be advantageously attained by injecting various materials into the rectum, so as by mechanical distention, or by irritating the mucous membrane, to stimulate the peristaltic action. The simplest, least irritant, and least active *enema* is one of cold water. In cases of habitual constipation, especially when complicated with piles, the injection of a pint of cold water at a fixed hour daily often acts most kindly. The ordinary *opening injection* consists of a pint of water, and a tablespoonful, each, of salt, molasses, and soft soap; castor oil is often added to it, and, if it be desired to make it very active, a teaspoonful of oil of turpentine.

Forced enemata.—The forced injection of large quantities of water for the relief of certain diseased conditions has long been employed in an irregular way; but the practice has become more common since Gustav Simon has proven the possibility of readily filling the large and even the small intestine, by forcing water into the rectums and through two patients suffering from intestinal fistula, the opening leading in the one case into the large intestine about the junction of the cæcum and ascending colon, in the other probably into the small intestine (*Archiv d. Klin. Chir.*, xv.). Recently Mosler has experimented on a patient in whom a finger introduced through the fistulous opening could feel the ileo-cæcal valve. Using a method to be shortly described, he found that in two minutes from the time water first entered the rectum it commenced to stream from the orifice, having traversed the whole length of the large intestines (*Berlin. Klin. Wochensch.*, No. 45, 1873).

Forced enemata are of especial value in *intussusception*, in which disease they have not rarely relieved the symptoms at once by mechanically distending and unfolding the invaginated gut. Dr. Mosler also commends them in *hernia*, and has employed them as *anthelmintics*. As such they are, of course, especially useful against the *oxyuris vermicularis*, which often inhabits the whole of the large intestines; but Dr. Mosler succeeded with them in removing a large *tape-worm*, probably from the colon. Especially in the case of the *seat-worm* the vermifugal enemata should be medicated; and probably the safest and most efficient substance for this purpose is quassia. Dr. Mosler used a tablespoonful of chlorine-water to every pint and a half of injection. In various *catarrhal* and other diseases of the large intestines, Dr. Mosler commends these large enemata as a means of cleansing the gut, removing acrid secretions or foreign matters, and applying local treatment. A. Röhrig (*Experim. Untersuch. ü. d. Physiol. der Gallenabsonderung*, Wien, 1873) having found that intestinal injections of water have a very great influence over the secretion of bile, Dr. Mosler has been led to try forced enemata in catarrhal and other *jaundices*, with asserted good results.

In administering these large injections a syringe should never be used. The apparatus to be provided consists of a rectal tube of hard rubber, with a conical point, below which are several good-sized openings; an india-rubber tube two feet and a half long fitted to the rectal tube, and a funnel. The patient should lie upon his back, with the hips elevated. The tube being introduced into the rectum, the free end with the funnel is raised vertically, and water poured into it. When it is desired to force fluid into the small intestine, much depends upon the introduction being performed slowly, and the patient should be placed upon his knees and shoulders, so that the pelvis may be much higher than the shoulder. It is essential that the tube be fitted with a cock, or be pinched, so as to regulate the passage of the liquid. In this way from five to nine pints are readily injected.

The indications to fulfil which cathartics are used are as follows:

1. *To unload the bowels.*—It is not necessary, in a work like the present, to say anything about the evil results of retained fecal matter, but only to point out the methods of relief. Before this can be done to advantage, however, a summary of the causes of *constipation* is required. Constipation may be well divided into acute and chronic. *Acute* or *temporary constipation* is that which occurs under special, transient circumstances, as in convalescence from acute disease, and in pregnancy. It is to be relieved by the use of laxative articles of diet, and, this not sufficing, by laxatives or purgative medicines. It should never be forgotten that acute constipation is sometimes due to organic affections of the alimentary canal, such as enteritis or intussusception, or is caused by mechanical obstacles, such as a hard foreign body or an enormous gall-stone. It is evident that such cases are not simple constipation; that the treatment required is essentially different from that of the latter affection, and is various according to the lesion. For the diagnosis and treatment of these diseases the reader is referred to works on the practice of medicine. *Chronic constipation* may be due to sedentary habits of life; to habitual overwork, especially of the nervous system; to a deficiency of intestinal secretion and of peristalsis, apparently natural to the individual and without obvious cause; to long-continued voluntary habit of restraining the desire to go to stool; tc lead or other forms of poisoning; and to diseases of the nervous system producing a paralytic state of the intestinal muscular fibres. It is evident that in the treatment of these various forms of constipation due regard must be paid to the cause, which should always, if possible, be removed. There are also certain cardinal principles which apply to the treatment of all forms of chronic constipation. They are as follows:

1. A voluntary effort at defecation is to be daily made at a fixed hour, whether the desire exist or not.

2. Medicines are to be avoided as far as possible, a sustained effort being made to regulate the bowels by means of diet.

3. In very many cases the daily use of enemata of cold water, with attention to diet, suffices to attain the desired result.

4. If medicines become necessary, as small an amount as will suffice, and the mildest drugs, are to be used. Purgatives or laxatives are at best merely temporary devices, and if abused in costiveness increase the trouble. So far as can be, the attempt should be to produce a permanent impression, an alteration of the intestinal glandular action or peristalsis. Thus, when atony of the muscular coat exists, strychnia, or, according to recent experiments and clinical observations, Calabar bean (see page 304), may be employed: if the hepatic or other glands are habitually torpid, nitro-muriatic acid may be administered.

When constipation is attended with low spirits and a coated tongue, it is almost always due to a deficiency of secretion, and may be looked upon as a form of dyspepsia: in such cases nitro-muriatic acid is especially valuable, but sometimes a mild mercurial course seems almost imperative.

A second use of cathartics under the present indication is to remove offending materials, as indigestible or irritant food, foreign bodies, acrid discharges, etc. For these purposes a brisk, quickly-acting purgative is generally best.

2. *To deplete.*—On account of the large serous flow which they produce, the hydragogue cathartics when freely exhibited cause a very decided general depletion.

Local depletion by means of cathartics is called for in *congestion* of the *portal circulation*, as well as in *dysentery* and other acute intestinal inflammations. Under the first of these conditions may, we think, be included without violence cases of the so-called "torpidity of the liver," which will be discussed in the article upon calomel. In acute *intestinal inflammations* the salines are to be preferred when depletion is desired, as they produce very large serous discharges and are not at all irritant.

3. *To promote absorption.*—By emptying the blood-vessels the cathartics favor the absorption of the exuded fluid in general dropsy. For this purpose the hydragogues, and especially elaterium, are the best purgatives. The production of catharsis is the surest method of relief in general *dropsy*, also in *ascites;* in other forms of local effusion its effects are less marked. As, however, purgation is the most exhausting of all the plans employed for the cure of dropsy, due regard must always be had to the strength of the patient. It is frequently necessary actively to support or even to stimulate while it is being carried out.

4. *To revulse.*—The long tract of the alimentary canal affords a great extent of surface upon which to practice revulsion in certain brain-diseases, as in *mania* and rheumatic or gouty *irritation* of the *cerebrum*. In *hyperæmia* of the brain, purgatives do good by depleting as well as by acting as revulsives. The drastics should be preferred.

5. *To eliminate.*—It cannot be doubted that the use of purgatives in such

diseases as fevers and cholera, with the idea of eliminating some *materies morbi*, rests simply upon a crude, unproven, and probably false pathology. In rheumatic disease and in gout it is more probable that they do good in this way, although it is by no means certain that the advantage derived from their use is not simply due to depletion. In cases of retained renal secretion, the evidence is very decided that they do aid in separating the products of retrograde metamorphosis from the blood.

6. *To influence the pelvic circulation.*—The only purgative used for this purpose is aloes, in the article upon which all that is necessary will be said upon the subject.

LAXATIVES.

As has been already stated, constipation should always, when possible, be overcome by laxative food. There are two qualities by virtue of which food is laxative. Chief of these is *bulk*. All aliment which contains a large amount of innutritious material affords a large residuum, which, by distending the intestine, stimulates peristalsis. Contrariwise, articles of diet which are highly nutritious and afford but little residuum are constipating. This holds good, more or less strictly, among the lower animals. Thus, the flesh-eating carnivora are habitually constipated; the grass-eating herbivora very generally lax. Owing to its containing so little of the innutritious portion of the grain, the finest white flour favors a costive habit, whilst the "cracked wheat," in which the whole grain is eaten, is laxative; as to a still greater degree is bran, which is composed almost wholly of the husk of the wheat, the least nutritious portion of it, and therefore leaves a large residuum after digestion. *Cracked wheat* is boiled into a sort of jelly-like mass, and eaten with cream and sugar, whilst *bran* is taken in the form of bran bread, bran crackers, or bran mush. *Unbolted flour*, containing the whole of the grain, is about equal to cracked wheat, and is often made into bread. *Indian meal*, in the form of cakes or of mush, is highly nutritious, and somewhat laxative; oatmeal is decidedly laxative, scarcely so much so as bran, but much more nutritious. When it agrees with the stomach, and is easily digested, it is probably the best of all these laxative articles of food. As the oats produced in warmish climates are very inferior, care should be taken to procure oatmeal manufactured from Northern grain. It should be thoroughly cooked, and is best eaten in the form of a thick porridge. In dyspepsia all of these articles sometimes disagree with the stomach and cannot be used.

Some dietary articles seemingly possess *dynamic* laxative powers,—*i.e.*, they exert a direct action which is not mechanical, but is similar to, although far less active than, that of the true purgatives. They intensify the intestinal action. Chief among substances of this class are *molasses* (*Syrupus Fuscus*, U.S.), and its congener, *brown sugar; white sugar* (*Saccharum*, U.S.) probably does not share these laxative powers; *sugar of milk* (*Saccharum Lactis*, U.S.) is probably also nearly inert. Of course, great care is usually necessary in taking advantage of the laxative virtue of molasses, on account of the danger of producing fermentation and acidity in the primæ viæ. An obvious deduction, however, is to encourage the use of brown instead of white sugar in those of constipated habit.

There are certain foods which combine the two methods of action spoken of. Chief among these are the fresh acidulous fruits—such as apples, pears, etc.—and the dried fruits. Of the latter, the fig (*Ficus*, U.S.) is one of the most palatable, and, owing probably to the great number of small seeds which it contains, is the most efficient. Prunes are nearly as agreeable as figs. To a limited extent the finest varieties of them may be eaten raw; but they are especially to be recommended stewed. When it is necessary, a pinch of senna-leaves may be cooked with them, and, if it be not made too large, increases the activity of the dessert without affecting its flavor.

Among constipating articles of diet, it is only necessary to call attention to milk as one of the most decided of the class.

The laxative remedies of the U. S. Pharmacopœia are as follows:

TAMARINDUS—TAMARINDS. U.S.

The preserved fruit of the Tamarindus Indica, a large tree, native of the East and West Indies. The fruit is a broad, compressed pod, usually from four to six inches long, somewhat curved, with an exterior brown hard rind. It contains seeds inclosed in cells formed of a tough membrane, between which and the rind is an acid pulp, the medicinal part of the fruit. Tamarinds are preserved for market by stripping off the outer rind, packing the inner portion in layers, and pouring on boiling syrup. In the market they are offered as adhesive masses composed of pulp, membranes, strings, and seeds, and having a sweet, acidulous taste. They contain a good deal of citric acid, much less of the tartaric, and a little of the malic acid. They are used chiefly in making refrigerant acidulous drinks for fever, and in convalescence as a laxative article of diet, half an ounce to an ounce or more being eaten like preserves. They enter into the officinal confection of senna.

MANNA—MANNA. U.S.

An exudation of the European ash, Fraxinus Ornus, chiefly produced in Sicily and Calabria. There are three varieties of it. The best, *flake manna*, occurs in unequal, rough, stalactite-like pieces with a crystalline or granular fracture, and is obtained in the hottest and dryest weather in July and August. The next quality, *manna in sorts*, consists of pieces of flake manna, mixed with a soft brownish matter; it is obtained in September. *Fat manna*, a soft viscous mass, which exudes during the wet weather in the latter part of October and in November, is the least valuable variety. Manna has a slight odor, a sweet, mawkish taste, and should contain from forty to eighty per cent. of the saccharine, active, crystalline principle *Mannite*, which differs from ordinary sugar in not containing equal parts of hydrogen and oxygen, and is therefore not readily convertible into grape sugar or its derivative, alcohol.

THERAPEUTICS.—Manna is a gentle laxative in large doses, sometimes causing flatulence and pain. It is rarely used by itself, but is added to infusions of more powerful purgatives, to cover their taste and aid in their effects. The laxative dose for an adult is half an ounce to two ounces; for a child, one to four drachms in an aromatic infusion.

CASSIA FISTULA. U. S.—*Purging Cassia* is the pulp of a hard, blackish, cylindrical pod from one to two feet in length and about an inch in diameter, having on one side a single and on the other a double dark band, running the whole length of the pod, and marking the positions where its valves are united. The pods are produced by a large tree, Cassia fistula, a native of Egypt and India. The dark, sweetish, acidulous, officinal pulp may be used as a laxative in doses of half an ounce, but is apt to cause griping. It enters into the confection of senna.

FRANGULA. U. S.—The bark of the *Rhamnus Frangula*, one of the buckthorns of Europe, is considerably used abroad as a laxative, and contains a crystalline principle, *franguline*, besides glucosides, of which *emodine* is also found in rhubarb. In this country it is employed very rarely, but the bark of the *Rhamnus Purshiana*, or *California buckthorn*, is very largely used under the name of *Cascara Sagrada*. It probably contains principles either identical with or allied to those found in the European bark. In many cases its fluid extract acts most happily as a laxative in *habitual constipation*, although sometimes it causes griping pains and irritation of the mucous membrane. The best results are usually to be obtained by giving from ten to fifteen drops of the fluid extract one or two hours after meals; rarely half a fluidrachm given at bedtime seems to suit better an individual case.

MAGNESIA—LIGHT MAGNESIA. U.S.
MAGNESIA PONDEROSA—HEAVY MAGNESIA. U.S.

The *heavy* and the *light* magnesia differ only in their physical characters, the particles being differently aggregated. The *carbonate of magnesium* (*Magnesii Carbonas*, U. S.) is manufactured by precipitating a solution of the sulphate of magnesium by one of the carbonate of sodium. If the two solutions be concentrated, the dense or heavy carbonate falls; on the other hand, if the solutions be dilute, the precipitate is a light carbonate. Heavy magnesia is obtained by calcining a heavy carbonate; light magnesia, by using a light carbonate. All of these substances are of a milk-white color, and occur in powder; the carbonate sometimes in very light cubical blocks. They are all practically insoluble in water, freely so in dilute acid, and in the presence of acids they both act as alkalies.

THERAPEUTICS.—Magnesia and its carbonate act in the same manner upon the human economy, being both antacid and laxative. For their purgative powers they are probably dependent upon the presence of acids in the primæ viæ, and hence their effects vary. They are sometimes taken as habitual laxatives by persons suffering from *acid dyspepsia;* but, as they are said at times to accumulate in the intestines and to do harm mechanically, this use of them should be discountenanced. They are very frequently employed in conjunction with Epsom salt, senna, or other of the more powerful purgatives, on account of their antacid properties. Their chief use is in acute *acid dyspepsia*, in *sick headache*, in some forms of *diarrhœa* with excessive acidity in children, in *gout*, *rheumatism*, and in various *cutaneous affections;* wherever, in a word, a laxative antacid is indicated.

ADMINISTRATION.—The dose of the carbonate is, for a child a year old, from five to twenty-five grains, according to the effect desired; for an adult, half a drachm to half an ounce; that of the magnesia is about one-fifth less.

SULPHUR.

Sulphur is officinal in three forms: SULPHUR SUBLIMATUM, or *Flowers of Sulphur;* SULPHUR LOTUM, or *Washed Sulphur;* and SULPHUR PRÆCIPITATUM, or *Precipitated Sulphur.* The first of these is made by subliming sulphur into cool chambers, and always contains some sulphuric acid, generated during the process. When freed from the acid by washing with warm water and ammonia, it constitutes the washed sulphur. The U. S. Pharmacopœia directs the precipitated sulphur to be prepared by boiling lime and sulphur together, so as to form a sulphide of calcium, and precipitating this with muriatic acid.

The sublimed and the washed sulphur occur as sulphur-yellow, crystalline powders; the precipitated as a whitish powder, whose particles are often coherent into friable lumps. For an account of the various allotropic forms of sulphur, and its chemical properties, the reader is referred to works on chemistry. It is insoluble in water, but soluble in alkaline solutions, in alcohol, the fixed and volatile oils, chloroform, ether, etc.

PHYSIOLOGICAL ACTION.—When applied locally, sulphur is almost without influence. Taken internally, it is dissolved to some extent in the alkaline intestinal juices and absorbed. It has been detected in the milk, sweat, urine, and even in the breath. It would appear to suffer oxidation in the system, at least its ingestion is followed by increase of the urinary sulphuric acid (Regensburger, *Centralb. Med. Wissen.*, 1877, 328). When in sufficient quantity, sulphur acts as a mild laxative, producing soft, semi-liquid, feculent stools, accompanied generally with much offensive flatus of sulphuretted hydrogen. It is affirmed that in some instances the latter gas has been so freely generated and absorbed as to cause systemic poisoning. Cases have also been reported in which the flowers of sulphur acted as an irritant poison; but this, without doubt, has been owing to their containing a large quantity of sulphuric acid. Its continued use has probably some effect upon nutrition; the secretions generally are slightly increased, and some have affirmed that the temperature is somewhat elevated; but the truth of this is certainly very doubtful. The results of clinical experience indicate that it has an especial tendency to act upon the skin and mucous membranes.

THERAPEUTICS.—As an habitual laxative, sulphur has been used with asserted advantage in cases of *hemorrhoids* and of chronic *rheumatism*. In subjects of the latter disease it is claimed that it exerts a beneficial alterative influence, especially in *sciatica* and in *lumbago* and other varieties of *muscular rheumatism*. It has also been employed as an alterative in various cutaneous affections; and in the form of natural sulphur-waters, used externally and internally, there is much testimony as to its value in both rheumatic and skin diseases. Sulphur is very largely used as a parasiticide in cases of *itch*. Dr. Tilbury Fox recommends its application in the following manner. He says, "I have applied to *all papules and vesicles* the following ointment: sulphur, half a drachm; ammonio-chloride of mercury, four grains; creasote, four drops; oil of chamomile, ten drops; and an ounce of lard. This is rubbed in night and morning for three days, especially to the interdigits and wrists; the same shirt is kept on till the third day, when it is changed and a warm bath given. The use of the parasiticide for two or three days should be followed by a good washing and the discontinuance of the remedy for a night. If the patient be not troubled with itching during the night, we may conclude that the acari are killed, and all we need to do is to guard against the hatching-out of fresh acari by the light application of our parasiticide once a day to any 'pimply' or itchy place for a few days longer, taking care that the foul clothes are well heated or scalded. 'Not too strong and not too long,' is my rule in the use of remedies for scabies. The occurrence of red, rough, erythematous patches is a sign that the remedy itself is creating a disease."

ADMINISTRATION.—Sulphur is generally given in powder, mixed with syrup or molasses. Dose, as an alterative, ten to twenty grains three times a day; as a laxative, one to three drachms at bedtime.

POTASSA SULPHURATA.—*Sulphurated Potassa* is prepared by heating together sulphur and carbonate of potassium. It occurs in liver-brown fragments, which form an orange-yellow solution in water. Its taste is acrid, alkaline, and very disagreeable. When moistened, it feebly emits the odor of sulphuretted hydrogen.

Locally applied, the sulphuret of potassium is a very decided irritant. Taken in large quantities, it is a violent corrosive poison, and is said to have produced fatal gastro-intestinal inflammation. In medicine it has until within a very short time been employed only externally. It has been used as a stimulating ointment (ʒss to ℥j) in various skin-affections, and is also used for the formation of sulphur-baths, the strength of which should vary, according to the requirements of special cases, from two to six ounces of the drug in thirty gallons of water. They should be taken warm, the patient remaining in from twenty minutes to two hours, and are said to cause a general excitement, amounting in some susceptible persons to high fever. When employed strong, they sometimes occasion a papular eruption. They have been used in *chronic rheumatism* and in various *scaly skin-diseases*.

CALX SULPHURATA. U. S. *Sulphurated Lime.*—In the *Lancet* for February, 1874, Dr. Sidney Ringer recommended in the most laudatory manner sulphide of calcium in frequently-repeated doses of a tenth of a grain in *boils* when they appear in successive crops, and in various *scrofulous* and other unhealthy *sores*, such as occur especially in children, also in scrofulous *glandular enlargements*. The value of the remedy has been confirmed by Duhring and others; it is often given in half-grain doses. The Calx Sulphurata of the Pharmacopœia contains not more than 36 per cent. of pure sulphide of calcium, but is the commercial article known by that name.

PURGES.

OLEUM RICINI—CASTOR OIL. U.S.

A fixed, nearly odorless oil, of a nauseous taste, obtained from the seeds of the Ricinus communis by expression. The seeds are slightly warmed before being put under pressure, so as to liquefy their contained oil; and the crude oil obtained from them is boiled with a small amount of water, so as to coagulate its albuminous impurities. The oil was formerly manufactured by means of alcohol, also by heating the seeds or by boiling them in water, and several varieties of it existed; but these are no longer in the market. Castor oil is remarkable for being soluble not only in ether but also in alcohol. The *castor-oil seeds*, or *beans*, as they are commonly called, contain an acrid fixed principle, which makes them exceedingly poisonous.

PHYSIOLOGICAL EFFECTS.—Castor oil acts upon the human organism as a mild but decided purgative, producing copious fluid fecal discharges, and in overdoses sometimes vomiting, and always purging freely. It is a matter of some doubt whether the properties of the officinal oil are or are not due to the presence of a minute quantity of the acrid principle of the seeds; although the probabilities are in favor of the affirmative proposition. That the oil or its active principle is absorbed is proven by analogy, and by the facts that in children it sometimes purges when rubbed upon the skin of the abdomen (Cauvane, quoted by Stillé), and that when taken into the stomach it has been known to exude from the skin (Ward's case, *London Med. Gaz.*, vol. x. p. 377). In regard to its existence in the stools, the testimony is conflicting. Thus, Bucheim (*Virchow's Archiv*, Bd. xii.), although he submitted the passages produced by it to careful chemical manipulation, failed to detect it or any of its derivatives in them; but Bird (quoted by Stillé) and other observers affirm that it can be seen by the eye in the dejecta, either as oil or in the form of caseous flakes. According to the experiment (quoted by Stillé) of Hale upon himself, half an ounce of castor oil injected into a vein produces malaise, nausea, faintness, anxiety, and general dulness and depression, without purging.

THERAPEUTICS.—On account of the mildness of its action and an especial property which it appears to have of soothing an irritated bowel, castor oil is constantly employed whenever it is desired simply to evacuate the intestinal canal; not so much, however, in *chronic constipation* as when a temporary action is alone required. In various inflammatory or irritative affections of the alimentary canal, castor oil is of the greatest service, partly, no doubt, by removing acrid irritating secretions or foreign materials, such as undigested food, and partly by causing a depletion of the congested vessels, but also apparently by virtue of an almost specific power, which renders it the most satisfactory cathartic in these cases. This is especially seen in the acute *diarrhœas* and even in the *chronic enteritis* of children, but also holds good in the *diarrhœas* and *dysenteries* of adults.

Within the last few years a good deal has been written in regard to the use of the leaves of the castor-oil plant as a *galactagogue*, and sufficient evidence has been brought forward to render them worthy of some confidence. A poultice made of the fresh leaves should be applied to the breasts, and a teaspoonful of a fluid extract, prepared from the same, should be exhibited three or four times a day.

ADMINISTRATION.—Castor oil is very repulsive to the palate, so much so as to nauseate, or even vomit, by its taste, some susceptible individuals. It has been the habit to administer it in emulsion with a strong mint-water, or to give it in the froth of porter or in a cup of hot coffee; but by far the best plan is to mix it with an equal part of glycerine and to add two or three drops of the oil of cinnamon or of gaultheria to each dose. The substances do not stay mixed, but separate on standing: when used, they may be made temporarily to recombine by shaking the bottle. As glycerine has feeble laxative power, an ounce of this mixture represents a little more than half an ounce of the oil. It should be taken directly out of the spoon. The full purgative dose of the oil is half an ounce to an ounce for an adult; for an infant a year old, one to two teaspoonfuls. In dysentery it is sometimes advantageous to give the drug in small dose every three hours until a decided purgative operation is induced.

TOXICOLOGY.—Although castor oil is harmless, yet the beans contain an acrid principle, which renders them exceedingly poisonous, three of the beans having sufficed to destroy the life of a man (*Med. Times and Gaz.*, May, 1861). The symptoms do not usually come on until from two to five hours after the ingestion of the poison, when severe abdominal pain is felt, accompanied by violent vomiting and by purging, which after a time may become bloody, and soon ushers in a stage of collapse, with or without severe muscular cramps, with cold sweating skin, contracted features, thirst, restlessness, small rapid pulse, and sometimes the general appearance of Asiatic cholera. After death, intense redness and even abrasion of the stomach and of the small intestines are found. The treatment should consist in the evacuation of the stomach and bowels by mild emetics, such as ipecacuanha and warm water, and by mild cathartics, such as castor oil, provided nature has not already sufficiently fulfilled the indications, and in the free use of opium and demulcent drinks, the early external application of leeches and of emollient poultices, and the swallowing of small pieces of ice: in other words, the treatment, after evacuation, should be that of acute gastro-enteritis.

HYDRARGYRUM. U.S.

The only preparations of mercury which are used as purgatives are *calomel* and *blue mass*. Of these the first is by far the more active, and indeed is the only one which can be relied upon to purge, since the pilulæ hydrargyri very frequently will, if given by themselves, fail to induce liquid stools.

The chief interest in the purgative action of mercurials centres in the question as to their influence upon the liver. The evidence at present derivable from experiments upon the lower animals has already been discussed, and the decision arrived at that it must be rejected.*

When calomel is given to a healthy man in moderate purgative doses, green liquid stools are produced, which, after larger doses, are replaced by brown passages. The color of these passages has always been supposed by clinicians to be due to the presence of bile; but recently it has been affirmed that the green tint is owing to a compound of the mercury itself. Although no chemical proof of the presence of the metal or its salt has, that I am aware of, been furnished, yet it can scarcely be doubted that mercury is present in the first passages produced by calomel. The question, evidently, is not, Is mercury ever present in the "spinach-stools"? but, Is it always present? or, in other words, Is it an integrant portion of them? The evidence is not so abundant upon this point as is desirable, yet seems sufficient to furnish a negative answer to the last question. Simon (*Animal Chemistry*, Sydenham Soc. Transl., vol. ii. p. 386) and Golding Bird (*London Med. Gaz.*, 1845, p. 801), in careful analyses, both failed to detect the metal; and, as the recognition of mercury is an exceedingly simple chemical problem, it seems impossible that these chemists could have overlooked the metal if it had been present. Simon's analysis was performed upon the fifth stool after the administration of a large dose of calomel. The passage was fluid, perfectly green, had no fecal odor, exhibited a mild acid reaction, and showed, under the microscope, a great number of mucous corpuscles and epithelium-cells. Ether extracted from the solid residue (obtained by evaporation) a considerable amount of fat, which had an acid reaction, contained cholesterin, and was colored by biliverdin. All the other substances, which were separated from the stool by water and alcohol, were more or less colored by bile-pigment. Bilin, bilifellinic acid, and biliverdin were found in large quantity.

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* For a very elaborate and careful review of the clinical evidence as to the action of calomel on the liver, see Dr. Thos. R. Fraser's paper in the *Edinburgh Medical Journal*, April, 1871.

The most satisfactory evidence is, however, that furnished by Michéa (*Lancet*, 1849, vol. i. p. 15), who examined chemically the fæces under four different conditions. First, the spontaneous dejections of six healthy individuals: no bile was detected. Second, green stools of three persons suffering from gastro-intestinal derangement: bile-pigment was found in one case only, and in that could not be detected after persistent vomiting had ceased. Third, calomel having been given to eight healthy persons, five men and three women, bile was readily demonstrated in the green passages produced in all of the subjects. Fourth, saline and resinous purgatives were given to five persons, but no bile could be detected in the liquid stools.

To the evidence brought forward in favor of the proposition that calomel given to healthy men causes an increased escape of bile from the alimentary canal, may be added the conclusive fact that in some persons, whose idiosyncrasies render them very susceptible to the action of calomel, it produces not merely purging, but also vomiting of bile, which is scarcely at all altered.

From the facts which have just been passed in review, the conclusion seems inevitable that mercurial purgatives given to healthy persons cause the escape of large quantities of bile from the alimentary canal.

As is well known, when from any cause bile does not pass into the duodenum, the stools become very pale, of a peculiar potter's-clay, or even white, color. Very frequently under these circumstances, which may co-exist either with diarrhœa or with constipation, mercurials will modify the color of the passages and alleviate or cure any symptoms present. In many cases the mercurials are, of course, powerless to effect the desired result; but this depends upon the cause being organic, or of some other nature not to be overcome by a mere stimulant to secretion.

As mercurials in health increase the flow of bile from the intestine, and as they will sometimes re-establish it in disease when the secretion has altogether ceased or has been very materially diminished, the conclusion seems to me inevitable that mercurials have the power of directly or indirectly increasing the secretion of bile. The only objection of any force to be urged against this deduction is founded upon the idea that the drug simply increases peristalsis in such a way as to cause the bile naturally in the duodenum to be swept out instead of being absorbed. The answer to this is embraced in the following facts: mercurials restore the color of the passages when pale from arrested secretion, often without producing diarrhœa; other even more active purgatives fail to induce the same bilious passages; when diarrhœa exists with clayey stools, the change in the color of the passages caused by a mercurial may coincide with a not increased, or even a lessened, amount of liquidity; diarrhœa ordinarily does not cause bile to appear in the passages.

THERAPEUTICS.—A mercurial purge is especially indicated by the congeries of symptoms known as "*biliousness*:" a heavily-coated tongue, bitter, disagreeable taste, heavy headache, depression of spirits, loss of appetite, slight nausea, and light-colored passages. It should be borne in mind that one or several of these symptoms may be absent in any individual case. Of all single indications for the use of calomel, the occurrence of *potter's-clay-colored* passages is the most important; and if such stools exist, and do not depend upon an organic cause, a mercurial should be given, whether there be constipation or diarrhœa.

In *bilious fever*,—*i.e.*, *malarial fever with congestion of the liver*,—a mercurial purge, or several mild mercurial purges, will often, by exciting the action of the hepatic gland, be of great service in preparing the way for or aiding in the action of quinine. In *catarrhal jaundice*, mercurials, on the whole, offer, I think, the most frequently successful mode of treatment. It is evident that in such cases calomel does good not merely by its cholagogue influence, but even to a greater extent by its antiphlogistic power, no doubt lessening the viscidity of the secretions and abating the inflammatory action in the hepatic ducts. In many instances it is well to exhibit a mercurial purge to start with; but the main reliance is to be placed in the continuous exhibition of small doses of the drug until the gums are rendered slightly sore. Anything like profuse salivation is, of course, to be avoided. In *dysentery* of an acute sthenic type, calomel has yielded, in my hands, better results than any other remedy. It probably acts as an antiphlogistic and as an alterative, not only to the liver, but to all the intestinal glands. In one or two cases of *obstructive enteritis*, with severe constipation, which I have seen treated with this drug after the failure of other remedies, improvement in the local and constitutional symptoms commenced simultaneously with slight ptyalism, and continued on to recovery.

RHEUM—RHUBARB. U.S.

The root of Rheum officinale, Baillon, and other species of Rheum growing in China, Chinese Tartary, and Tartary.

Rhubarb occurs in hard, irregularly cylindrical or roundish pieces, of a brownish-yellow color, peculiar bitter taste, and imparting to the teeth a sense of grittiness, due to the presence of great numbers of minute crystals of the oxalate of calcium. There were formerly two chief varieties in market, the *Russian* and the *Chinese*. The first of these was the best, and was distinguished by the exterior of the pieces being cut or pared with a knife, and by a conical hole, evidently made for inspection with the point of a sharp instrument, and never reaching beyond the centre of the mass. The cause of the superiority of this brand of rhubarb was the close governmental inspection which it received on the Russian frontier. Such pieces as failed to pass the officials found their way into commerce through Turkey, and constituted the so-called *Turkey Rhubarb*, which resembled the Russian in external characters, but was of somewhat inferior quality. The *Chinese Rhubarb* was distinguished by the outside of the pieces having been scraped, and by the existence of a large hole running clear through and often retaining a portion of the cord upon which the roots had been strung to dry. Owing to the expiration and non-renewal of the treaty between the governments of Russia and of Tartary, the only officinal variety of rhubarb now in the market is the Chinese. Besides the true officinal varieties from Asia, there is a drug in commerce which from its source is known as *European Rhubarb*. It occurs in long, cylindrical pieces, or very often is cut to imitate one of the varieties of the genuine drug, from which it is to be distinguished by its more spongy texture and by the complete or almost complete absence of grittiness when chewed.*

The active principles of rhubarb have not all been made out; it certainly contains chrysophanic acid, and a peculiar tannic acid, to which it owes its astringency. *Chrysophanic Acid*† crystallizes out of alcohol in orange-yellow, golden, shining needles; out of benzole in orange-yellow or pale six-sided rhombic plates; with nitric acid it produces a fine yellow color; with the alkalies, a beautiful purple-red. According to Schlossberger, Bucheim, Meykow, and Auer, it is not purgative; but Schroff has found it to be so.‡ It certainly is not the chief purgative principle of the drug. The substances known as *Rhein* and *Rhabarbarin* are complex bodies.

PHYSIOLOGICAL ACTION.—Rhubarb is somewhat stomachic, tonic, actively purgative, and, owing to its tannic acid, secondarily astringent, leaving a decided tendency to constipation after the primary purgation. Owing probably to its chrysophanic acid, it gives a yellowish color to the milk of nursing women and to the urine. Rhubarb urine is to be distinguished from that of jaundice by its becoming purplish-red on the addition of an alkali. Rhubarb is asserted to affect chiefly the muscular coat of the bowels, and to purge by increasing peristalsis; but I have never met with any proof of this common belief.

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* In the past, the European rhubarb has been considered of little value; but recently it has been claimed that it is as good as the Asiatic. See *U. S. Dispensatory*, 13th ed., p. 735; also Prof. Radius (*Apotheker Zeitung*, Bd. vi., 1871).

† Under the names of *Goa Powder* and of *Araroba* or *Chrysaroba* have long been used in Brazil and the East Indies certain powders, varying from fine to coarse and from a light yellow to a dark chocolate, which are now known to be identical, and the product of a Brazilian tree. They depend for their activity upon *chrysophanic acid*, of which Squier states they frequently contain as much as sixty-five per cent. Dr. I. Ashburton Thompson has found that from six to eight grains of this acid taken internally, after about four hours produce vomiting, sometimes repeated at intervals and sometimes followed by purging (*British Med. Journ.*, May, 1877). The slowness of the results he believes to be due to the difficulty of absorption. The only practical application of the Goa powder or its active principle is in certain skin diseases, especially in *psoriasis*. According to the researches of Dr. Balmano Squier, its power in this disorder is extraordinary. He uses an ointment made by dissolving the acid in hot lard (gr. v to ʒij in ℥i), cooling, and mixing thoroughly with a pestle. The ointment sometimes produces excessive irritation, hence it is advised to commence with a strength of not more than twenty grains to the ounce, well rubbed in twice daily. The acid stains of a dark purple; this can be removed from hair, underclothes, etc., by hot benzole, if no soap or alkali has been used. The skin and nails are said to contain enough of potash to set the dye.

‡ See *Die Pflanzenstoffe*, p. 985.

THERAPEUTICS.—Notwithstanding its astringent property, rhubarb is largely used as a habitual laxative, because it does not impair, but, on the contrary, seems to strengthen, the appetite and the digestion. It should not be used in a high sthenic state of the system, or when depletion is necessary, but is, on the other hand, the best purgative when it is desired simply to unload the bowels in a debilitated subject. In *diarrhœa*, with intestinal weakness or relaxation, it is the best purgative with which to unload the bowels of acrid secretions retained in them; and in the form of the *aromatic syrup* combined with an alkali it is especially valuable in the *summer bowel-complaints* of children when the stools are greenish and mucous.

ADMINISTRATION.—Rhubarb is seldom employed in powder, but, when used, may be given in the dose of twenty grains. In chronic constipation, small pieces of the root are very often carried in the pocket and chewed by the person affected *pro re nata*. The U. S. Pharmacopœia recognizes the following preparations: *Extractum Rhei*, dose, five to ten grains; *Pilulæ Rhei*, each containing three grains of rhubarb; *Pilulæ Rhei Compositæ* (two grains rhubarb, one and one-half grains aloes), dose, two to four pills; *Pulvis Rhei Compositus* (rhubarb and magnesia), dose, half a drachm to a drachm; *Extractum Rhei Fluidum*, dose, twenty to thirty minims; *Syrupus Rhei*, dose, for an infant, a fluidrachm; *Syrupus Rhei Aromatica*, dose, for an infant, a fluidrachm; *Tinctura Rhei*, dose, one to two fluidrachms; *Vinum Rhei*, dose, one to four fluidrachms; *Tinctura Rhei Aromatica*, dose, half to one fluidrachm; *Tinctura Rhei Dulcis*, dose, two to three fluidrachms. The aromatic preparations are of pleasant taste and efficient.

JUGLANS. U. S.—The inner bark of the Juglans cinerea, or common butternut, or white walnut. Juglans is said to be a mild cathartic, resembling rhubarb in its action, as a substitute for which it was introduced during the Revolution by the famous Dr. Rush. The dose of the *extract* (*Extractum Juglandis*, U. S.) is twenty grains.

ALOE—ALOES. U.S.

There are three commercial varieties of aloes, which are all obtained in a similar manner,—*i.e.*, by cutting off the thick succulent leaves of the various plants, standing them up, allowing the juice to drain into suitable vessels, and afterwards inspissating, either by exposure to the sun or by slowly evaporating. The leaves contain a very large amount of a thick mucilaginous juice, which escapes on pressure: hence aloes prepared by expressing the leaves or by boiling them—both of which processes are sometimes practiced—is very inferior. *Socotrine Aloes* is the product of Aloe Socotrina, which grows in the island of Socotra in the Indian Ocean, and on the southern coast of Arabia. It alone is recognized by the U. S. Pharmacopœia. *Barbadoes Aloes* is prepared in Barbadoes and other West Indian islands, from the Aloe vulgaris. *Cape Aloes* is obtained at the Cape of Good Hope, from the Aloe spicata.

Aloes are darkish extracts, of a bitter nauseous taste, yielding their virtues to alcohol, imperfectly to water, and very perfectly to alkaline solutions. The Cape aloes is said to be "characterized by its dark-olive or greenish-black color, its smooth and very glossy surface when broken, its translucency at the edges, and the fine bright-yellow color of its powder, which is slightly tinged with green." The Socotrine aloes is distinguished by its yellowish-brown or reddish-brown color, its translucent edges, agreeable aromatic odor, and beautiful golden-yellow powder. The Barbadoes aloes is characterized by its dark-brown or reddish-brown color, its dull fracture, opaque edges, disagreeable nauseous odor, and dull olive-yellow powder. Of these varieties the Socotrine is most esteemed in human medicine. The Barbadoes is said to be the strongest, but is employed almost exclusively in veterinary surgery.

Messrs. T. and H. Smith (*Chemical Gaz.*, 1851) in 1850 discovered in Barbadoes aloes a crystalline principle,—aloin,—which was shortly afterwards found by Pereira to exist already crystallized in the sap of various species of aloe plants, and was subsequently obtained by Groves (*Pharm. Journ.*, xvi.) from Socotrine aloes. *Aloin* crystallizes from its watery solution in sulphur-yellow granules, from a hot alcoholic solution in star-like groups of needles. It is neutral, odorless, of a taste at first sweetish, afterwards intensely bitter; soluble with difficulty in cold, freely in boiling, water and alcohol. The statements regarding the purgative properties of aloin are exceedingly contradictory, some physicians finding it a drastic purge in doses of one or two grains, others declaring that fifteen grains of it have no effect, whilst others affirm that it is a mild purge. It is evident either that there are several substances described and used under the same name, or else aloin owes its purgative properties to some impurity that adheres to it closely.*

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* Consult *Chem. Gaz.*, 1851; *Die Pflanzenstoffe*, p. 1047; *Trans. Brit. Pharm. Soc.*, 1872, *Brit. Med.*, i., 1887, p. 747; *Bull. Thérap.*, xci., p. 259; *Lond. Med. Record*, 1877, p. 459; *Edinb. Med. Journ.*, xx., p. 1002; xxii., p. 1087. Dr. Fronmüller (*Med. Chir. Centralb.*, Wien, 1879, xiv.) says that one to three grains of Merck's aloin dissolved in hot water administered hypodermically acts as an efficient purge; whilst Dr. R. Kohn affirms that he has used both aloes and aloin of three different commercial varieties hypodermically without effect, giving ten times the dose employed by Fronmüller. In the lower animals Dr. Kohn found the hypodermic injections to cause gastro-enteritis with albuminous urine, and a peculiar inflammation of the kidneys: 0.1 grm. of Merck's aloin for every kilogramme of bodily weight was found to be a fatal dose for the dog. Aloin could be detected in the urine. (Method of analysis given.) *Schmidt's Jahrb.*, cxciv. 246.

PHYSIOLOGICAL ACTION.—Aloes is a stomachic, stimulant cathartic, remarkable for the slowness of its action. It has been supposed to influence chiefly, if not solely, the large intestine, and the clinical evidence is very strong that in overdoses it produces irritation of the rectum. The belief, formerly so universal, that it is capable of producing hæmorrhoids, has been very much weakened by the researches of a number of modern observers, among whom may be mentioned Trousseau and Pidoux (Stillé, *Therapeutics* vol. ii. p. 444). Its habitual use in large doses is said to cause tenesmus, a feeling of weight, heat, and uneasiness in the pelvis, and occasionally excitation of the sexual organs. Although I have used it a good deal, however, I have never seen these results. It undoubtedly has a tendency to increase the menstrual flow. Aloes is certainly absorbed, as is shown by the fact attested by Dr. Gerhard (*North American Med. and Surg. Journ.*) and other observers, that it will purge when its powder is sprinkled upon a blistered surface. In regard to its action in combination, Prof. Stillé states that when other and quickly-operating cathartics are taken along with aloes it does not appear to modify their action; but if it is administered seven or eight hours before a saline or other active purgative, a combined and very powerful operation is the result.

THERAPEUTICS.—Aloes in small doses is one of the best remedies for *constipation* of atonic subjects, especially when a stomachic stimulant is indicated. In these cases it may often with great advantage be combined with a simple bitter, one or two grains of it taken directly after meals being generally sufficient. In the constipation of plethora it should not be employed; neither should it be administered when active abdominal or rectal inflammation exists. During pregnancy it may be used as a laxative, but, unless some especial indication calls for its use, it is best avoided. Large purgative doses of it should never be given to pregnant women, as it certainly irritates the pelvic organs, and is even said to have the power of causing abortion. Formerly it was taught that aloes should not be used in *hemorrhoids;* but most, if not all, of the cases of this affection depend upon a condition of relaxation of the rectal veins, and Dr. Fordyce Barker (*American Practitioner*, 1872) insists upon the great value of aloes in piles, and states that Oppolzer was especially famous for his treatment of this affection, and that his prescriptions were, when piles are associated with constipation, aloes and quinine; without constipation, aloes and sulphate of iron. For bleeding piles he used ℞.—Ferri sulphat., ℈i; ext. aloës aq., ʒi; ext. taraxaci, q. s. Ft. pil. no. 60. S.—One morning and evening, and increase to three a day if necessary. When costiveness accompanies atonic *amenorrhœa*, aloes alone of all the laxatives should be exhibited; and it is also of service in atonic *menorrhagia.*

ADMINISTRATION.—Aloes is very rarely or never used by itself to produce free purgation, but may be given in the dose of from ten to twenty grains; in the dose of from three to five grains it is a decided laxative. As aloes often contains sticks and other extraneous matters, the U. S. Pharmacopœia directs that an *Aloe Purificata*, or *Purified Aloes*, should be made by dissolving the crude drug in alcohol, straining, and evaporating. The preparations are: the *tincture* (*Tinctura Aloes*,—1 to 10, U. S.),—dose, as a laxative, one to three teaspoonfuls; the *tincture of aloes and myrrh*, *Elixir Proprietatis* (*Tinctura Aloes et Myrrhæ*,—aloes and myrrh, āā 1 to 10, U. S.), dose, as a laxative, one to two teaspoonfuls; the *wine* (*Vinum Aloes*, —6 to 100, U. S.), which contains also cardamom and ginger,—dose, as a laxative, one-half to one teaspoonful; the *pills* (*Pilulæ Aloes*, U. S.), which contain each two grains of aloes and two grains of soap; the *Pills of Aloes and Asafetida* (*Pilulæ Aloes et Asafœtidæ*, U. S.), useful in costiveness of hysterical or old subjects, each pill containing four grains of a mass composed of equal proportions of aloes, asafetida, and soap; the *Pills of Aloes and Mastich* (*Pilulæ Aloes et Mastiches*, U. S.), the famous "*Lady Webster Dinner-Pill*," each containing two grains of aloes; the *Pills of Aloes and Myrrh* (*Pilulæ Aloes et Myrrhæ*, U. S.), used in amenorrhœa, and containing two grains of each ingredient in every pill; the *Pills of Aloes and Iron* (*Pilulæ Aloes et Ferri*, U. S.), containing each one grain of aloes and one of dried sulphate of iron.

SENNA—SENNA. U. S.

The leaflets of the shrubs Cassia acutifolia and C. obovata, of Nubia and Upper Egypt, and of C. elongata, of Southern Arabia. The senna leaves vary from three-fourths of an inch to an inch and a half in length, and are to be distinguished by the inequality of their bases, the two sides of the lamina or leaf-blade joining the midrib at unequal heights and angles. There are three commercial varieties of senna, which are named from the places of their export. *Alexandria Senna*, the most common variety, is distinguished by the presence of the shorter *argel-leaves*, with equal bases, by the ovate-pointed leaflets of Cassia acutifolia, and by the scattered mucronate-obovate leaflets of C. obovata. *India Senna* is characterized by the oblong leaflets, from one to two inches in length, entire and perfect. *Tripoli Senna* may be recognized by the great extent to which the leaflets are broken up. The active principles of senna have not been completely isolated, but appear to be several. *Cathartic Acid*, discovered by Draggendorff and Kubly (*Viertel-jahresschrift für Prakt. Pharm.*, Bd. xvi.) is undoubtedly actively cathartic, as Kubly found that fifteen grains of it dissolved in an alkaline solution produced in six hours frequent watery discharges, with griping; but the researches of Bourgeois and Bouchut (*L'Union Pharmaceutique*, Nov. 1871) indicate that, besides cathartic acid, there are in senna chrysophanic acid, and a purgative principle which has not as yet been isolated. The *cathartine* of the older writers is undoubtedly a complex body.

Physiological Action.—Senna is a very powerful cathartic, producing watery fecal discharges, and acting, it is said, as readily upon swine, dogs, cats, and horses as upon man. According to Prof. Stillé, both Courten and Regnaudot found that its infusion injected into the veins caused vomiting and purging. It is undoubtedly absorbed; and Bergius affirms that it will impart its purgative property to the milk of nursing women.

THERAPEUTICS.—Whenever a brisk, somewhat irritating cathartic is desired, senna may be selected. When given alone, it is very apt to gripe severely, and is consequently more often used in combination,—especially its infusion with Epsom salt (*Black Draught*). In obstinate *fecal accumulation* the Black Draught constitutes a most efficient and safe remedy. It is claimed that senna does not leave a tendency to constipation after its action; and hence, in small doses, it is preferred by some as an habitual laxative.

ADMINISTRATION.—Whenever senna is exhibited, an aromatic should be united with it, to lessen its tendency to gripe. The leaves are not given in substance. The dose of the *fluid extract* (*Extractum Sennæ Fluidum*, U. S.) is two fluidrachms to half a fluidounce; the *confection* (*Confectio Sennæ*, U. S.) is a very complex but elegant preparation, used only as a laxative, in doses of one to two drachms, especially in *pregnancy*, and not suited to dyspeptic cases, on account of its tendency to derange the digestion. *Infusum Sennæ Compositum*, U. S. (*Black Draught*), contains manna and sulphate of magnesium,—a very active hydragogue purge, dose, four fluidounces; the dose of the *syrup* (*Syrupus Sennæ*, U. S.) is one to four fluidrachms; the *Pulvis Glycyrrhizæ Compositus*, U. S., or compound liquorice powder, is an excellent pleasant laxative in doses of thirty to sixty grains.

Euonymus, U. S., or *Wahoo*, the bark of the Euonymus Atropurpureus, is, according to the experiments of Prof. Rutherford, an active cholagogue in dogs, and given in the form of the fluid extract, or of the solid resinoid extract, *euonymin*, its effects are often most happy in cases of *habitual constipation* and *hepatic torpor*. It acts very slowly and purges only moderately. The dose of the fluid extract is a dessert- to a tablespoonful; of euonymin, two to four grains: in cases of *dyspepsia* it may be repeated with good results two or three times a week. The dose of the *extract* (*Extractum Euonymi*, U. S.) is three to six grains.

SALINE PURGATIVES.

MAGNESII SULPHAS, U. S.—*Sulphate of Magnesium*, or *Epsom Salt*, is now manufactured on a large scale from dolomite, the double carbonate of calcium and magnesium, and from native siliceous hydrite of magnesium. Sulphate of magnesium ordinarily occurs in small, acicular, slowly-efflorescent crystals, containing about fifty-one per cent. of water of crystallization, soluble in their own weight of water at ordinary temperatures. By proper precautions, it may be obtained in large quadrangular prisms, terminating in a four-sided pyramid or a dihedral summit. The taste is bitter, saline, nauseous.

Physiological Action.—Epsom salt is a most active hydragogue cathartic, producing very large watery discharges without causing any irritation of the intestines. In very large doses it is, however, capable of producing fatal hypercatharsis; and Christison reports the case of a boy ten years old, said to have been killed by two ounces of the salt, without the induction of purgation. Injected into the veins of the dog or rabbit it is a deadly poison, causing death by failure of respiration, and also depressing the heart (Dr. J. H. Recke, *Inaug. Diss.*, Göttingen, 1881; also Dr. M. Hay).

Therapeutics.—Whenever, in inflammation, it is desired to deplete through the bowels, the sulphate of magnesium offers the most advantageous method of doing it. Especially is this the case when the intestines are affected, as in *enteritis* or in *colitis*. There is probably no other purgative in common use which produces at the same time such free serous evacuations and so little intestinal irritation. On account of the efficiency of its action and the watery character of its discharges, it is especially applicable to cases of *fecal accumulation* and of obstinate *colica pictonum*. The dose is half an ounce to an ounce, properly diluted. Recently the hypodermic use of the sulphate has attracted some attention. M. Luton has found that ten centigrammes (1.53 gr.) administered in this way usually provoke several watery stools (*Gaz. Hebdom.*, 1874, p. 455).

Liquor Magnesii Citratis, U. S.—*Solution of Citrate of Magnesium* is prepared by putting into a strong bottle a syrupy solution of the citrate of magnesium containing an excess of citric acid, adding the bicarbonate of potassium, and corking tightly. On account of its agreeable taste and effervescence, this preparation is much used as a purgative. It is similar to Epsom salt in its action, but is less efficient, more apt to gripe, and more irritating. It ought not to be used in inflammatory affections of the bowels.

Magnesii Citras Granulatus, U. S.—*Granulated Citrate of Magnesium* contains less free acid than the solution, and is therefore somewhat less pleasant to the taste. The dose is one to three teaspoonfuls taken in solution whilst effervescing.

Sodii Sulphas, U. S.—*Sulphate of Sodium*, or *Glauber's Salt*, is at present manufactured from common salt by means of sulphuric acid. It occurs in six-sided, very efflorescent, striated prisms, which finally crumble into a white powder. Its taste resembles that of Epsom salt, but is more nauseous. On this account, and because its action upon the economy is similar to but harsher than that of the sulphate of magnesium, in human medical practice it has been completely superseded by the latter salt. The dose is a quarter of an ounce to half an ounce, properly diluted.

Sodii Phosphas, U. S.—*Phosphate of Sodium* occurs in colorless, transparent crystals, which effloresce and become opaque on exposure. It is a tribasic phosphate, one part of water acting as a base. It is soluble in four parts of cold water, and has a saline taste, closely resembling that of common salt. In large doses it is said to be a mild saline purgative, but as such is at present very rarely used. Within a few years the use of the phosphate of sodium in chronic infantile diarrhœa has attracted a good deal of notice. Originally recommended, so far as I know, by Dr. Routh, in his work on Infant-Feeding, as being a valuable nutrient or alterative in children, attention has been especially drawn to the phosphate of sodium by Dr. William Stephenson (*Edinburgh Med. Journ.*, 1867, vol. xiii. p. 336). He believes that it acts upon the liver, and adduces much clinical evidence in favor of his views. The cases in which he especially recommends it are "infants who are being artificially reared, and who are liable to frequent derangement of the bowels; also when the phosphatie elements in the food seem deficient; where, from the character of the motions, there is a deficient or defective secretion of bile. It is thus of service in cases of chalky stools or white fluid motions, and in many cases of green stools; also in duodenal dyspepsia, and in diarrhœa and weaning." Dr. S. G. Webber (*Boston Med. and Surg. Journ.*, 1868, vol. i. p. 5) confirms these statements of Dr. Stephenson, and in a few cases I have seen very notable effects from this use of the drug.

Potassii et Sodii Tartras, U. S.—*Tartrate of Potassium and Sodium*, or *Rochelle Salt*, is made by the addition of the carbonate of sodium to a solution of the bitartrate of potassium. It occurs in large, colorless, transparent, slightly efflorescent, prismatic or half-prismatic crystals, which are soluble in two and a half parts of cold water, and have a slightly saline taste. It is a mild saline purgative, decidedly less efficient, but much less offensive to the palate, than Epsom salt. The dose is from half an ounce to two ounces, properly diluted.

Pulvis Effervescens Compositus, U. S.—*Seidlitz powder* is in two packets, the white paper containing thirty-five grains of tartaric acid, the blue paper forty grains of the bicarbonate of sodium and two drachms of Rochelle salt. When they are taken, the powders are dissolved separately, the solutions added, and the whole drunk whilst effervescing. They are very acceptable to the stomach, refrigerant and laxative rather than purgative. Seidlitz powders are used almost exclusively to evacuate the bowels, and exhibited after blue mass to "carry off" mercurials, etc. They should be taken on an empty stomach, as before breakfast. One powder is the usual dose; but not rarely even two powders will fail to purge.

Potassi Sulphas, U. S.—*Sulphate of Potash*, or *Vitriolated Tartar*, was formerly used as a purgative, but is no longer employed in medicine, except in the preparation of Dover's powders.

The *Sulphovinate of Sodium* has recently been brought forward as a substitute for Epsom salt. A very great advantage is claimed for it, in that it has a refreshing flavor with very slight bitterness, and when given in flavored syrups makes a very pleasant drink. Its action is said to be rapid and thorough. The dose is two to four drachms for children; four to six drachms for an adult.

DRASTICS.

As already stated, the *drastics* are those vegetable cathartics which are actively irritant. With perhaps one or two exceptions, in sufficient amount they are capable of causing fatal gastro-intestinal irritation. The line between the drastics and the stronger purgatives is, of course, placed more or less arbitrarily, since the various cathartics differ in action almost by insensible degrees. Thus, jalap, although included among the drastics in this work, might with perhaps even greater propriety be classed among the purgatives, since it is very little more active or irritant than is senna. Further, these remedies in combination seem to lose, in a measure, their power of causing irritation, and to become useful purgatives. A fact, however, which makes the classification here employed clinically useful, although it be not scientifically accurate, is that none of these remedies should be used when a purgative is desired to relieve gastro-intestinal inflammation or irritation; and, on the other hand, when a revulsive action is wished for, as in some cases of brain-disease, one of the drastics should always be selected.

JALAPA.—JALAP. U.S.

The tuber of Exogonium purga, a convolvulaceous vine growing in Mexico. Jalap comes into the market in two forms: one, that of the younger roots, which are sold undivided; the other, that of the old roots, which are brought into the market in transverse or longitudinal slices, and in pieces. The first variety consists of very hard, irregularly globular, brittle roots, about the size of a shut fist, or smaller, and often slashed with vertical incisions, made for the purpose of facilitating drying. The section of jalap is always distinctly resinous, if not to the naked eye, at least to the vision aided by a lens. The active principle is a duplex resin, one portion of which is soft, and soluble in ether, the other (*Rhodeoretin*) hard, and insoluble in the latter menstruum. Rhodeoretin is asserted by both Kayser and Mayer (*U. S. Dispensatory*) to be the purgative principle; but Mr. J. C. Long (*Amer. Jour. of Pharm.*, 1861) has shown that the soft resin is equally active. The percentage of resin varies very much in different specimens, but is much greater in those that are worm-eaten.

PHYSIOLOGICAL ACTION.—Upon dogs and horses jalap (Stillé, *Therapeu-*

tics, vol. ii.) is said to act as a powerful hydragogue cathartic, and in overdoses as a gastro-intestinal irritant. If the experiments of Cadet de Gassicourt be correct, it probably acts by absorption, as, according to that observer, diarrhœa may be produced in dogs by its free application to the shaven skin. Prof. Stillé, however, asserts that it does not impart its purgative properties to the milk of nursing women, and that in man it is not absorbed by the skin. In man jalap produces free hydragogue catharsis, often with nausea; or, if in overdoses, violent vomiting and purging.

THERAPEUTICS.—Jalap is especially indicated when it is desirable to produce large watery stools. It is, however, very rarely used alone. A favorite combination with many practitioners is of it and calomel. In the form of the *compound powder* (*Pulvis Jalapæ Compositus*, U. S.,—jalap, thirty-five parts, cream of tartar, sixty-five parts), jalap is very frequently used with great advantage in *ascites* and also in other forms of general *dropsy*. It is believed when given in this way to exert some influence upon the renal functions: for very many cases the proportion of cream of tartar in the officinal compound powder is too small, and should be increased.

ADMINISTRATION.—The dose of powdered jalap is ten to twenty-five grains, of the *abstract* (*Abstractum Jalapæ*, U. S.), five to thirteen grains. The *resin* (*Resina Jalapæ*, U. S.), like the other purgative resins, is prepared by precipitating a saturated tincture with water. According to Husemann, the ordinary adulterations of jalap resin may be detected by the solubility of the substances employed in the oil of turpentine, which does not affect the genuine article. On account of its tastelessness, this preparation, as well as the similar one of scammony, is sometimes employed as a purgative for children. The dose for an adult is from two to four grains.

COLOCYNTHIS—COLOCYNTH.

The fruit, deprived of its rind, of the Citrullus Colocynthis, or bitter cucumber, a vine growing in the Cape of Good Hope, Japan, Syria, Egypt, Turkey, the islands of the Grecian Archipelago, etc. The fruit is a round gourd, from two to four inches in diameter, of a whitish or pale-yellow color. It occurs in the market with or without its rind. The pulp is dry and membranous, whitish, and contains the active purgative glucoside *Colocynthin*, first discovered by Herberger.

PHYSIOLOGICAL ACTION.—The experiments of Orfila and Schroff have shown that upon dogs and rabbits colocynth acts very much as it does in man, producing copious watery evacuations, and, although not so irritant as gamboge, in overdoses causing death by gastro-intestinal irritation. If the statement of Richter that violent purgation may be induced by rubbing the abdomen with tincture of colocynth be true, the active principle is without doubt absorbed.

THERAPEUTICS.—Colocynth is rarely, if ever, used alone, but is given in combination with the other drastics, or with milder purgatives, to increase their activity. It is frequently added in small quantity, with advantage, to laxatives, especially when the constipation is somewhat obstinate. Its minute bulk is often of great advantage in these cases. Neither colocynth nor any of its combinations should be used in *dropsy*. Its chief use is, as a laxative, to unload the bowels, and to deplete directly from the portal circulation: even in cases offering these indications it is almost never used alone.

TOXICOLOGY.—Colocynth has not rarely produced death, preceded by hypercatharsis and the usual symptoms of gastro-intestinal irritation. The fatal dose probably varies very much. Christison records the death of a woman twenty-four hours after taking a teaspoonful and a half of the powder. Roques chronicles a fatal result produced by less than a drachm of the powder in decoction, but, on the other hand, narrates a case in which three drachms failed to kill (Husemann, *Handbuch der Toxicologie*, p. 625).

ADMINISTRATION.—Colocynth is used only in the form of the *extract* (*Extractum Colocynthidis*, U. S.); useful as an addition to laxatives,—dose, as a purgative, three to five grains; and of the *compound extract* (*Extractum Colocynthidis Compositum*, U. S.), which contains extract of colocynth, sixteen parts, purified aloes, fifty parts, resin of scammony, fourteen parts, cardamom, six parts, soap, fourteen parts, and is a very useful purgative preparation, either as a laxative in minute dose (one to three grains), or in large dose (five to twenty grains) as an active purgative.

SCAMMONIUM—SCAMMONY. U. S.

A resinous exudation from the root of the Convolvulus Scammonia, a vine growing in Syria. It is said to be obtained by cutting off the root obliquely about two inches from the origin of the stems, and catching in shells the few drachms of milky juice which exude from each root. From these shells it is emptied into a vessel and allowed to concrete. Before exportation it is usually adulterated with the expressed juice of the leaves and stalks, and with chalk, flour, ashes, sand, etc. This adulteration was formerly carried to a very great extent, but is at present indulged in to a much less degree. The pure or *Virgin Scammony* is in irregular, rough, fissured masses, of various sizes, commonly solid, with a dull resinous fracture, and of a dark greenish color, inclining to black. The smell is peculiar, resembling that of old cheese. The taste after a time is acrid. *Factitious* or adulterated scammony occurs in cakes of various sizes and shapes, and is sometimes spoken of as *amylaceous* or *cretaceous* scammony, according to the material used for its adulteration. The active principle of scammony is a resin, very similar to that of jalap. The proportion of this resin in the drug varies, according to the purity of the article, from eight to ninety per cent. The U. S. Pharmacopœia directs that scammony shall contain seventy-five per cent. of the resin.

THERAPEUTICS.—Scammony acts upon the system like jalap, but is somewhat more irritating, and therefore more apt to gripe severely, and is still more strongly contra-indicated in inflammatory diseases of the intestinal canal. It is decidedly less drastic than gamboge. It is never used alone, but in combination with other less active cathartics. The dose of the resin (*Resina Scammonii*, U. S.) is two to five grains.

As all of the ingredients have been noticed, the present seems the proper place for the consideration of PILULÆ CATHARTICÆ COMPOSITÆ, U. S.—*Compound Cathartic Pills.* These popular pills contain each: compound extract of colocynth, one and a third grains; abstract of jalap and calomel, each one grain; gamboge, one-fourth of a grain. As there is soap in the first ingredient, the calomel is sooner or later reduced to the black oxide of mercury.

The compound cathartic pills are a very efficient purgative, generally not producing much griping. They cause large watery stools, and are used when it is desired to empty the bowels and deplete from the portal circulation.

PODOPHYLLUM—PODOPHYLLUM. U.S.

The rhizome of the Podophyllum peltatum, or May-apple, a perennial herb, growing in the Northern and Middle United States. Podophyllum occurs in simple or branched, cylindrical, brownish pieces, about the thickness of a goose-quill, smooth or wrinkled longitudinally, often obscurely marked with the scars of leaf-scales, and furnished with numerous rootlets or their remnants attached to the lower surface. The taste is bitterish, acrid, nauseous. The rhizome contains the alkaloid *Berberina*, but the purgative power resides in two resins, one soluble, the other insoluble, in ether.*

PHYSIOLOGICAL ACTION.—The experiments of Dr. Snow, of Dr. S. R. Percy (*American Med. Times*, vol. iv.), of Dr. F. E. Anstie (*Med. Times and Gaz.*, March, 1863), and of others, have shown that, whether administered by the mouth or hypodermically, podophyllum produces in the lower animals purging, with colicky pains and sometimes vomiting. If the dose be sufficient, the stools are bloody, and after large amounts death occurs, preceded by hypercatharsis, prostration, and slight convulsions. On post-mortem examination, Dr. Anstie found intense inflammation, with ulceration of the mucous membrane of the small intestines. Upon man podophyllum acts as upon these animals, producing in large doses violent catharsis, accompanied by much pain, and is probably capable of acting as a fatal gastro-intestinal irritant. Ten grains produced in a strong woman violent bilious but not bloody vomiting and purging, with collapse, but final recovery (*Philad. Med. Times*, xii. 520). The experiments already alluded to show that it acts by being absorbed, which is confirmed by the experience of Dr. Percy, who found that its application to an ulcer was followed by its specific effects. It has been claimed that it acts especially upon the liver; and much clinical testimony has been adduced to support this view, which is also confirmed by the experiments of Rutherford (see p. 488).

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* Podowyssotzki states (*Arch. Exper. Path. u. Pharm.*, xiii. 40) that he has isolated a crystalline substance (*Podophyllotoxin*) which he believes to be the active part of podophyllin. One-tenth of a grain of it in a cat produced fatal vomiting and purging. By the action of an alkali it is resolved into two substances, *pikropodophyllin* and *podophyllinic* acid, which also exist in the rhizome. Pikropodophyllin resembles podophyllotoxin in its action upon the organism, but is less powerful. Dr. D. O. Brau has used podophyllotoxin as a purgative for children, and finds it to completely represent podophyllin. To a child thirteen years old he gives from six- to nine-hundredths of a grain (*Arch. f. Kinderheilk.*, ii. 1880).

Very large doses are distinctly poisonous. A child four years old was killed in this city by an unknown amount. The symptoms were repeated vomiting, slight purging, collapse, and finally coma, ending in epileptiform convulsions (Dr. T. G. Morton). An infant twenty-two months old recovered from four grains (*Australasian Med. Gaz.*, ii. 237).

THERAPEUTICS.—Podophyllum acts as a purgative like jalap, but more slowly and more continuously, and is more apt to produce "bilious discharges" and griping pains. In this country it is very largely used in cases of *acute constipation*, and with very good effect; and it has also been commended very highly by numerous practitioners in the so-called "*bilious attacks.*" Owing to the extreme slowness of its action, it is not well adapted for combination with brisker cathartics. The same quality fits it, however, for use with calomel, it requiring nearly the same length of time as that drug to produce purgation. L. Lewis (*Brit. Med. Journ.*, 1876, ii., p. 546) affirms that in small repeated doses (gr. $\frac{1}{40}$, t. d.) it is a powerful stimulant of the gustatory nerves.

ADMINISTRATION.—Although an *extract* (*Extractum Podophylli*) is officinal, podophyllum is scarcely ever given in other form than that of the resin, commonly known as *Podophyllin*. *Resina Podophylli* (U. S.) is prepared by precipitating a concentrated tincture with water: as berberina is soluble in the latter menstruum, the resin as thus obtained is free from the alkaloid. The portion of this duplex resin which is soluble in ether is certainly more actively purgative than the other part, to which, indeed, any purgative property is denied by some. Dose, as a purgative, from one-sixth to one-fourth of a grain; as a laxative, one-twelfth of a grain.

ELATERIUM.

A substance deposited by the juice of the fruit of the Momordica Elaterium, or squirting cucumber, a native of Greece, but cultivated in England. In the interior of the ovate fruit is an elastic sac, which contains the seeds and at ripening becomes so distended with juice that when the fruit falls off the vine, and the support is removed from the stem end, a rupture occurs at the latter position, and the liquid with the seeds is forcibly projected. The elaterium is said to be contained only in this inner juice. In order to avoid loss, the fruit is picked with a piece of the stalk adherent to it before ripening, and is opened by slicing. *Elaterium* occurs in light, friable, slightly incurved, greenish-gray cakes about a line thick. The taste is acrid and bitter; the fracture finely granular. Owing to the variability of commercial elaterium, the U. S. Pharmacopœia now recognizes only the active principle, *Elaterin* (*Elaterinum*, U. S.), which was first separated in a pure state by Morries (*Repertor. für Pharm.*, xxxix. 134). It crystallizes in colorless, shining, rhombic, six-sided, odorless tables, of a very bitter sharp taste and neutral reaction. According to Dr. H. Köhler (*Virchow's Archiv*, Bd. l. p. 287), it is insoluble in water and glycerine, readily soluble in cold alcohol, and soluble with difficulty in ether and turpentine.*

PHYSIOLOGICAL ACTION.—Locally applied, elaterium is a very decided irritant, producing, according to Pereira, ulcerations in the fingers of those who handle the fruit and prepare the drug for market. When taken internally, it acts on man as a most powerful hydragogue cathartic, producing, when the dose and administration are properly regulated, enormous watery stools, without much irritation. On the lower animals its action is much less certain. Viborg asserts that a horse was unaffected by a pound of elaterium fruit; and I have given one and even two grains of a presumably active elaterium to a dog without producing very obvious results. If the dose be sufficiently large, all animals probably are, however, fatally affected by elaterium, perishing by progressive depression. Prof. Stillé asserts (*Therapeutics* vol. ii. p. 459) that the death is not rarely preceded by violent vomiting and purging; and even when these are absent during life, post-mortem examination reveals congestion and inflammation of the gastric and intestinal mucous membranes. In none of my own experiments, which have not been very numerous, has any purging been present; further, in Dr. Köhler's elaborate investigation (*loc. cit.*), elaterium dissolved in alcohol was injected under the skin, the powdered elaterium was put into the rectum, and was given by the mouth after the gall-duct had been tied so as to prevent the flow of bile into the intestine, and in neither case was there any purging, but prostration, apathy, disturbed respiration, salivation, and violent convulsions, ending in death. From these experiments Dr. Köhler draws the conclusion that elaterium exerts a general action upon the system, for which its introduction into the blood is all that is requisite, and also a purgative influence, for which it is necessary that there be bile in the duodenum to dissolve the elaterium and cause it to act locally on the intestine. The objection to this conclusion is that our present light seems to indicate that elaterium does not purge dogs and rabbits, even when given under ordinary circumstances. Further, there is considerable evidence to show that elaterium applied externally will cause purging in man (see Stillé, *Therapeutics*, vol. ii. p. 459). If this be true, the application of the conclusions arrived at by

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* For the behavior of it with various reagents, and for the methods of searching for it in medico-legal investigations, the reader is referred to Dr. Köhler's memoir.

Köhler to man certainly would be incorrect. Köhler's experiment proved that in animals elaterium is absorbed, even when given by the mouth, since he found it in the urine of the poisoned dogs and rabbits.

THERAPEUTICS.—Elaterium is certainly the most efficient of all the hydragogue cathartics, producing in properly-regulated doses the freest evacuations with comparatively little pain and irritation. It is therefore indicated whenever a powerful cathartic of such nature is indicated. It is the most efficient of all the medicines of the class in general *dropsy* or in *ascites*. As, however, its action is very exhausting, great care should be exercised not to give it in too large doses, and also to support the strength of the patient during the period of purgation, and afterwards by alcoholic stimulants, easily-digested nutritious food, and appropriate hygienic measures. In the latter stages of dropsy the injudicious use of elaterium may favor, and no doubt has accelerated, the fatal result, by intensifying the exhaustion. An idea has prevailed that elaterium is especially valuable in *uræmia*, because it produces an elimination of the urea in the stools; but I have been unable to find authority for the asserted elimination. Be this as it may, however, clinical experience has demonstrated the utility of elaterium in chronic renal disease. In order to deplete, elaterium has been employed in various diseases; but this use is not to be encouraged, and especially when there is any gastro-intestinal irritation or inflammation are the salines much preferable to elaterium. In cases of plethora, however, when there is a sudden *determination of blood to the head* and a very powerful impression is needed, the vegetable cathartic may be advantageously employed.

TOXICOLOGY.—Elaterium is without doubt capable of destroying life, and that, too, when not in large quantity. I know of but one recorded death,—that of a woman who took, by the advice of a quack, two and two-fifths grains of the extract of elaterium and sixteen grains of rhubarb. Violent and uncontrollable vomiting and purging came on, and proved fatal in thirty-six hours. After death, the gastro-intestinal mucous membrane showed marked evidences of inflammation. (See *Beck's Medical Jurisprudence*, 12th ed., vol. ii. p. 719.)

ADMINISTRATION.—It is not safe to commence with more than one-sixth of a grain of elaterium, to which should be united a grain of the extract of hyoscyamus and a drop of some aromatic oil. The dose of the officinal elaterinum is one-twentieth of a grain; of the *trituration* (*Trituratio Elaterini*—1 to 10, U. S.), one-half a grain.

CAMBOGIA—GAMBOGE. U. S.

A gum resin, obtained in Siam by breaking off the leaves and young shoots of the tree known by botanists as the Garcinia Morella, and catching in suitable vessels the juice as it drops. When the receptacles consist of hollow bamboos, the juice hardens into cylindrical casts, striated externally, and with a central cavity due to the loss of substance in drying. This is the so-called *pipe gamboge*. *Gamboge in sorts* occurs in irregular masses. Gamboge is a hard, resinoid substance, of a brittle, often conchoidal fracture, of a deep reddish-orange color on exposed surfaces, more yellowish when freshly broken, affording a bright-yellow powder, insoluble in water, with which it forms, however, an intensely yellow emulsion. It has little or no taste, but when chewed produces, after a time, an acrid sensation in the fauces. It contains, according to Christison, as much as seventy-two per cent. of *gambogic acid*, a resinous acid of a cherry-red color, forming red salts with alkalies. This would appear, however, to be only one of the purgative principles of the drug, since it is less drastic than an equal weight of gamboge (Christison, *Ann. Chem. Pharm.*, xxiii. 185; Pabo, *Additam. quæd. ad Virtutes chem. et physiol. Resinarum quarundam comparatas*, Dorpat, 1851; Daraszkiewicz, *Meletemata de Resinarum, præsertim Resinæ Gutti, in Tractu Intestinali Rationibus*, Dorpat, 1858); five grains producing in some persons only watery evacuations, in others not even these, and as much as seventeen grains having been taken without more serious effect than severe purgation.

Physiological Action.—Administered by the mouth to dogs, cats, horses, and probably other of the lower animals, gamboge acts very generally as a violent drastic cathartic; but from the experiments of Schaur and of Orfila it would appear to cause sometimes simply vomiting, and, when in very large amounts, death, without any marked symptoms other than those of progressive depression. In such cases the gastro-intestinal mucous membrane was found highly inflamed, and the intensity of the irritation probably paralyzed the intestinal functions. According to Daraszkiewicz and to Schaur, in order for gambogic acid to act as a purgative the presence of bile in the intestine is necessary. As it has been determined by Schaur (quoted by Husemann, p. 754) that the hypodermic administration of gamboge to dogs results simply in the production of local abscesses, and as A. L. Richter asserts that when applied to raw surfaces in man it acts simply as a local irritant, it would appear at first sight that gamboge does not act by absorption. This is, however, probably not true, the alkaline juices of the alimentary canal probably dissolving it so that it can readily be taken up by the villi. Further, both Gmelin and Tiedemann assert that they have found its principles in the urine. Schaur has, however, been unable to detect it in the urine of persons or of animals taking it. Even when he injected large quantities of it into the blood of dogs, he failed to find it in the urine, although he did obtain a resinoid substance which he believes to be a derivative of gambogic acid. Lewis, Abeille, and Ferriar assert that, when given in certain ways, gamboge acts as a decided diuretic. If this be true, absorption of it must occur.

Therapeutics.—On account of the intense irritation which large doses of it produce, gamboge is very rarely, if ever, used alone as a purgative, but is employed to give sharpness to purgative combinations. In very obstinate *habitual constipation* it has been used in doses of one or two grains as a decided laxative. Its use as a hydragogue in *dropsy* is to be absolutely condemned, it being much less effective for this purpose, and more irritating, than various other substances. The dose of gamboge is from two to five grains, made into pill with soap, or given in alkaline solution.

OLEUM TIGLII—CROTON OIL. U.S.

The fixed oil obtained from the seeds of the Croton Tiglium, a euphorbiaceous shrub of Hindostan and other portions of Southern Asia. This oil is quite viscid, and varies in color from a pale yellow to a dark reddish brown, and has an acid reaction. Its taste is hot, acrid, and extremely persistent; its odor faint, but peculiar. The composition of croton oil is very complex, and the active purgative principle has not as yet been separated. The most important of the substances so far discovered in the drug is that found by T. Schlippe and named by him *Crotonol.* According to this investigator, it is not the purgative principle, although to it the drug owes its power of causing a peculiar dermal inflammation.

Physiological Action.—Locally applied, croton oil is an intense irritant, producing upon the skin an eruption which is at first papular, but in a very short time becomes pustular. This effect of the drug will be considered more in detail under the heading of Counter-Irritants. When given by the mouth, croton oil acts upon the horse, dog, and probably other mammals, as upon man, producing violent purging, with severe griping, and, when in sufficient amount, fatal gastro-intestinal inflammation. The question as to whether it acts by producing a simple local impression or by absorption is unsettled. In the experiments of Hertwig (Stillé, *Therapeutics*, 2d ed., vol. ii. p. 449) and of Bucheim (*Virchow's Archiv*, xii. 1), purgation did not follow the injection of the oil into the veins of animals; but Conwell obtained a result contrary to this, and there is considerable testimony that its external use in man is sometimes followed by its specific effects upon the alimentary canal (Stillé, *Therap.*, 2d ed., vol. ii. p. 451). The probabilities seem to me to be in favor of the purgation being due to the absorption of the oil.

Therapeutics.—Croton oil is a very rapidly-acting, violent drastic and hydragogue cathartic. It is chiefly used in cases of *obstinate constipation* from disease of the nervous system or from lead-poisoning. The fact that a drop of it placed upon the tongue will purge actively, peculiarly fits it for use in *mania*, *delirium tremens*, and other diseases when the patient refuses to take medicine. When it is desired, as in some brain-diseases, to revulse through the bowels, croton oil is probably the most available of the cathartics. The dose is one drop, which may be administered in pill, emulsion, or by simply placing upon the tongue. In overdoses, croton oil is a violent poison.

Toxicology.—Although in small amounts croton oil causes such severe symptoms, yet in larger quantities it has failed to produce as serious results as would be naturally expected. It is, however, very possible that in at least some of these recorded cases the oil was adulterated. Cowan has reported a case (Husemann, *Toxicologie*, Bd. ii. p. 443) of a child, four years old, who recovered in two days from a teaspoonful of croton oil taken on a full stomach; Adams (*Ibid.*) saw recovery in an adult after the ingestion of a drachm, and in the *Boston Med. and Surg. Journ.*, 1868, i. 294, is recorded the case of a woman who took about an ounce, was vomited forty-five minutes afterwards with mustard, and finally recovered. The minimum fatal dose is not known, and probably varies very much. A child aged thirteen months was killed by a quantity believed not to exceed three minims (*Med. Times and Gaz.*, 1870, i.). Giacomini (Stillé, *Therapeutics*, vol. ii. p. 451) reports a case in which twenty-four grains of the drug proved fatal in as many hours: although there were but four stools, the patient presented the symptoms of general collapse, preserving consciousness to the last: a little less than two drachms have caused vomiting and death without purging (*Amer. Journ. Med. Sci.*, April, 1874).*

HELLEBORUS NIGER.—Black hellebore is the root-stock of the Helleborus niger, a native of Southern and Middle Europe. It contains two active medicinal principles, *Helleborein* and *Helleborin*. Both of these substances are glucosides. According to Marmé (quoted by Husemann), helleborein is an active cardiac poison and a drastic purgative, whilst helleborin, although having to some extent the latter property, acts chiefly as a narcotic, producing in animals at first inquietude, soon followed by paresis both of motion and of sensation, constantly deepening after large doses into death.

Black hellebore when taken by man is said to cause, if in sufficient quantity, violent catharsis, with vomiting, abdominal pains, cramps, and convulsions, which have ended fatally. Locally applied, the fresh root is a violent irritant. It has been used in times past as a hydragogue cathartic, but appears to be both uncertain and very harsh in its action, and, in this country at least, is never used at present. The *extract* and the *tincture* are purgative in doses of ten grains and two fluidrachms respectively.

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* For other cases, see *Med. Gaz.*, vol. xliii.; *Edinburgh Med. Journ.*, 1861; *Lancet*, 1870 i.; *Brit. Med. Journ.*, 1874, i.; *Ann. d'Hyg.*, 1871, i.

CLASS III.—DIURETICS.

Diuretics are medicines used for the purpose of increasing the flow of urine. Some of them, without doubt, act directly upon the secreting structure of the glands, but others of them induce the increased secretion indirectly, by, in some way, removing the obstacle to secretion. It is notorious that diuretics often fail in practice when their action is most urgently needed. This results, in many cases, from the nature of the disease, and is not because diuretics are powerless or uncertain. Thus, in cardiac disease the congestion of the kidneys may be so great as to render secretion impossible; and it is equally evident that when the tubules are destroyed by Bright's disease medicine must be powerless to provoke excretion.

There are certain agencies whose influence upon the kidneys should never be lost sight of in exhibiting diuretics. Thus, cold, by checking the secretion of the skin, often acts as a most efficient remedy of the class, and, whenever a diuretic action is urgently needed, it should be employed as an adjuvant to the medicinal substances.

Again, mere vascular fulness tends to provoke excretion of water by the kidneys. This assertion does not rest simply upon theory. In an elaborate series of experiments, E. Roux (*Archives Physiol.*, 1874, p. 578) found that the ingestion of large quantities of water greatly increased the flow of urine, but did not sensibly affect the elimination of urea or uric acid, although the elimination of the chlorides seemed to be augmented; in Böcker's (*British and For. Med.-Chir. Rev.*, xiv., 1854) experiments, however, large draughts of water increased not only the amount but also the solids of the urine. The recent investigations of J. Meyer (*Hoffmann und Schwalbe's Jahresb.* 1881, 345) explain these discrepancies and show how water may be of service in various diseases. He found that at times, when the tissues were full of the products of disintegration, the effect of water in increasing elimination was very marked, but that upon the wasting processes of the body the water exerted no influence. It would seem, therefore, that whilst we cannot by water produce tissue disintegration, we can wash out by it the retained products of tissue change, and I cannot help suspecting that the great rarity of uninherited gout in America has some connection with the universal habit of drinking water very freely. The taking of large draughts of simple water at regular intervals has been found to act very favorably in *acute Bright's disease*, greatly increasing the urinary flow, and at the same time lessening the irritation of the kidneys. In various inflammations or irritations of the genito-urinary organs, as in gravel, whenever it is desired to make the secretion less irritating or less concentrated, the value of water as an adjuvant to medicinal diuretics should always be taken advantage of.

There certainly is a very marked antagonism between the bowels and the kidneys, so that free catharsis reduces very decidedly the secretion of urine. There is also an antagonistic relation between the skin and the kidneys, so that an increase in the excretion from one of these generally results in a diminution of that of the other emunctory. This should also be taken advantage of when a diuretic action is desired. Sweating and purging at such times are therefore to be avoided. When a diuretic is exhibited, the patient should be kept cool, walking about if able, or if it is necessary for him to remain in bed he should be covered lightly. Not rarely, a remedy which when administered cold and the patient kept cool afterwards will act as a diuretic, when given hot and the patient kept warm will act as a diaphoretic.

There are various substances which are of such nature that when eliminated by the kidneys they act upon the mucous membrane of the bladder and other surfaces over which they pass. It seems hardly correct to speak of these drugs as diuretics; yet they are best considered in the present class.

The chief indications for the use of diuretics are as follows:

1. *To maintain the action of the kidneys.* It is hardly necessary here to discuss the necessity of excretion to the system. In various kidney diseases this indication is very urgent; but as the lessened excretion too often depends upon a profound organic alteration of the renal secreting structure, it is evident that very frequently diuretics must fail when most needed. In the great majority of cases in which diuretics are used to fulfil the present indication, only the mildest of the class should be employed. Whenever there is inflammation of the kidneys, even if it be chronic, the stimulating diuretics should be avoided. When lessened urinary excretion is purely functional in its origin, diuretics are often most serviceable. In fevers especially is it necessary to maintain the action of the kidneys; for this purpose water should always be freely given during fever. The alkaline diuretics sometimes may be exhibited; but the most generally serviceable of all remedies of the class in these diseases is the sweet spirit of nitre.

2. *To evacuate fluid.* For this purpose diuretics are employed in all forms of dropsy, and are successful in direct proportion to the universality of the effusion and the structural perfection of the kidneys.

3. *To soothe and diminish irritation of the genito-urinary organs.* The value of water in fulfilling this and the next indication has already been pointed out. By lessening the acidity of the urine and rendering soluble the uric acid which is present, the alkalies are equally important in carrying out the present and the following indication.

4. *To alter the urinary secretion so as to prevent the deposition of calculous material.* Notwithstanding it has been claimed otherwise, I think it

indubitable that as yet no practical measure has been devised of dissolving a calculus when once formed. Even to alter the urine so as to prevent further deposition is probably impracticable, except in cases of uric acid diathesis. A discussion of the use of diuretics for this purpose will be found in the article on Potash, which is the only diuretic used to meet the present indication.

Diuretics are very naturally divisible into three sets,—the hydragogue diuretics, the refrigerant diuretics, and the stimulating diuretics. These classes, of course, run more or less into one another, but are sufficiently distinct for practical purposes. The drugs belonging to the first set simply increase the flow of water from the kidneys, and are therefore used chiefly for the relief of dropsy; those of the second division exert a marked sedative action upon the system,—very generally do not increase to a great extent the water of the urine, but mostly modify the secretion in one way or the other. They are used in dropsy to alter the urinary secretion, and for their sedative and eliminative action in acute disease. Diuretics belonging to the third division are of such nature that their active principles are eliminated by the kidneys, and act upon the mucous surfaces over which they pass; for which purpose they are chiefly employed.

HYDRAGOGUE DIURETICS.

SCILLA—SQUILL. U.S.

The bulb of Scilla maritima, a liliaceous plant growing in the south of Europe, especially on the shores of the Mediterranean. The bulb varies in size from that of a child's head to that of the fist. It is composed of numerous layers or scales, which separate when it is sliced for drying. As kept in the shops, squill is in horny flakes, of a white or red color, becoming leathery when wet, and having an acrid bitter taste. It yields to water and alcohol, and also to vinegar. *Scillitin* has been asserted to be the active principle of squill; but the *scillitin* of different authors is diverse. According to Reil, there are two active principles in squill, one of which he names *scillitin*, representing the diuretic and expectorant properties of the drug, whilst the toxic and irritant properties reside in a substance which he calls *sculein*; very recently (*Arch. Exp. Path. und Ther.*, xi. 22) C. V. Jarmersted[*] has described a new principle from squill (*Scillain*), and Merck has sold three substances as derived from squill,—*scillin*, *scillipicrin*, and *scillitoxin*.[†]

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[*] Jarmersted states that his scillain increases, and afterwards diminishes, blood-pressure, causes vomiting and purging, and finally paralyzes the heart-muscle.

[†] Dr. Fronmüller has reported (*Memorabilien*, 1879, xxiv. 250) a series of experiments made, upon persons suffering from various ailments, with the scillin, scillipicrin, and scillitoxin of Merck. He found that the scillitoxin in doses of 0.45 grain acted as a rather uncertain diuretic, and frequently caused giddiness, headache, and loss of appetite; scillin seemed to be devoid of diuretic properties, whilst a gramme of a solution of scillipicrin in water (one part in fifty) administered hypodermically usually invoked a great flow of urine, without other evil symptoms than some smarting at the place of injection.

Physiological Action.—According to the experiments of Chateau (quoted by Stillé) and of Marais, squill in poisonous dose produces in dogs and other of the lower animals vomiting, then purging, dulness, stupor, intermittent paralysis, convulsions, and finally death in the course of twelve or fifteen hours. The temperature always falls. Recently, Prof. Schroff (*Wochenblatt der Zeitsch. der k. k. Gesellsch. zu Wien*, 1864, p. 424) has re-investigated this subject, using alcoholic extracts of the red and white squill, and also the scillitin of Merck. Fifteen grains of the latter caused in a vigorous rabbit great weakness, mydriasis, and, after an hour or so, tremors gradually becoming violent, partial stupor, labored breathing, and finally death; twenty-three grains caused in another rabbit sinking of the pulse and respiration-rate, mydriasis, diuresis, and death, preceded by the other symptoms noted in the previous case. The alcoholic extract (fifteen grains) caused (*loc. cit.*, 424) in a large rabbit decrease of the number of respirations per minute, with rise of the pulse-rate, narrowing of the pupil, semi-stupor, and finally death. On post-mortem examination of rabbits killed with the scillitin, erosion of the gastric mucous membrane, pericardial and sub-pleural hemorrhages, pulmonary apoplexy, bloody urine, and hyperæmia of the kidney and brain were found. In rabbits destroyed by the extract, gastric erosion and the various hemorrhages were wanting. It seems evident that the scillitin of Merck does not represent squill. In a recent memoir, which I have only seen in abstract, Dr. Husemann states that the extract of squill has no expectorant properties, that it acts on the heart like digitalin, that its diuretic powers are dependent upon its action on the circulation, and that both in large and small doses it uniformly produces a rise of temperature (*Deutsche Med. Wochens.*, No. 13, 1875; abstracted *Lond. Med. Rec.*, 1876, p. 120). Husemann also finds commercial scillitin very uncertain. These statements receive confirmation, at least in part, from the researches of C. Lupinski, who has found that scillitoxin is a powerful stimulant to the peripheral vagi in the frog, causing slowing of the pulse, and in certain doses diastolic cardiac arrest, and in the dog slowing of the heart. Large doses cause in the frog tetanic contractions of the heart. He also found that in the dog large doses finally paralyze the peripheral vagi and produce a rapid pulse. The arterial pressure is increased, partly, it is affirmed, by the increased cardiac energy, and partly by a peripherally produced vaso-motor contraction (*Hoffmann und Schwalbe's Jahrb.*, 1883, 123; from the Russian).

Clinical experience has established the fact that in small repeated doses squill is diuretic as well as expectorant. The remedy is evidently a stimulant to the kidneys, and in overdoses causes an irritation whose result is lessening of the secretion, scanty bloody urine, or absolute suppression of urine, according to the ingested dose of the poison. Its diuretic action has been noted in animals by Schroff and by Chiarenti (quoted by Stillé), and there can be no doubt as to the power that squill has of increasing the watery portion of the urine. I know of no studies upon its action on the urinary solids.

That the active principles of squill are absorbed is proven not only by its action on the kidneys, but also by the fact that its characteristic effects on the system have been seen to follow its external application. (See Stillé. *Therapeutics*, 2d ed., vol. ii. p. 534.)

In man, overdoses of squill produce violent vomiting, colicky pains, purging, and diminution or suppression of the urine, which may contain blood.

THERAPEUTICS.—As a diuretic, squill is in great repute, and is especially employed in cases of dropsy where the condition of the system is atonic and where there is no disease of the kidney. Profs. Wood and Chapman recommend it very strongly in cases of *serous effusion* into the *pleura* or the *pericardium* dependent upon chronic inflammation of the membrane. In these cases it may often be advantageously combined with calomel. The combination of squill and digitalis is very efficient in *cardiac dropsy*. The one contra-indication to the use of squill is the existence of any form of Bright's disease or of acute irritation of the kidney.

TOXICOLOGY.—Overdoses of squill produce violent purging and vomiting, with abdominal pain, lessened or almost suppressed secretion of bloody, albuminous urine, very marked reduction of the pulse-rate, ending, it may be, in collapse, convulsions, and death. According to Husemann (*Toxicologie*, Bd. i. p. 413), twenty-four grains of it have brought about a fatal result. The treatment consists in the evacuation of the stomach and bowels by ipecacuanha and castor oil, if nature has not already fulfilled the indication; the free use of opium; the exhibition of large quantities of water, for its action on the kidneys; and the usual measures for the relief of gastro-enteritis, if much tenderness be present. Early in the poisoning care should be exercised in the exhibition of alcoholic stimulants, for fear of increasing the gastric irritation; during the stage of collapse they may be imperatively demanded, and with their use should be combined that of dry heat applied externally, and of the other usual measures of relief during collapse.

ADMINISTRATION.—As a diuretic, squill should be given in solid form, two grains every two hours, the dose being gradually increased until some nausea is felt. The preparations of squill are the *tincture* (*Tinctura Scillæ*, —1 to 6.6, U. S.),—dose, ♏x to ♏xx; the *vinegar* (*Acetum Scillæ*—1 to 10, U. S.),—dose, ♏x to ♏xx; the *syrup* (*Syrupus Scillæ*, U. S.),—dose, fʒss to fʒi; the *fluid extract* (*Extractum Scillæ Fluidum*, U. S.),—dose, ♏i to ♏iii.

DIGITALIS, in its general relations, has already been sufficiently discussed, and it remains only to speak of its employment as a diuretic. In the first place, it should be distinctly understood that it has no alterative effect whatever, either upon the nature of the secretion or upon the mucous membrane over which that secretion flows. In other words, when it has any effect it is purely a hydragogue diuretic, simply increasing the watery portion of the urine. That digitalis has direct diuretic properties cannot, I think, be doubted. Nor does it seem less certain that it varies greatly in their exercise, so that when given to persons in health it will sometimes produce free diuresis and will at other times fail to do so. Another point to be constantly borne in mind during its administration is the fact that, like all the other actions of digitalis, diuresis is very slowly induced, and is very persistent when produced by the ordinary cautious method of administration. The diuresis of digitalis is not simply a result of its action on the circulation, since it will sometimes appear before the circulation is sensibly affected. At the same time, it is very evident that in disease the good effect of digitalis upon the renal organs is often in large measure due to its action upon the heart. Thus, in dropsy from a dilated heart the renal gland-cells cannot act because they are not supplied with the proper kind and quantity of blood, because their circulation, like that of the remainder of the body, is nearly stagnant. If under these circumstances digitalis be exhibited, and the circulation becomes comparatively free and active, the result is diuresis wrought out through a double mechanism, partly indirectly and partly directly produced by the drug. As a consequence of these facts, the clinicians have long since practically determined that digitalis is especially valuable as a diuretic in *cardiac dropsy*. Digitalis is, however, also very useful in *renal dropsy*, both in the subacute and the chronic form. Of course, like everything else, it frequently fails in these varieties of Bright's disease, but certainly it should always be tried. Prof. George B. Wood asserts that he has seen cases of "what appeared to be decided and obstinate attacks of Bright's disease, with universal dropsy, and unconnected with scarlatina, which yielded completely and permanently to the use of digitalis." In *acute suppression of urine*, digitalis is often a very valuable remedy when applied externally, especially when the stomach refuses to retain medicines. At the same time, it should be remembered that large doses of the drug used in this way sometimes induce very alarming symptoms. Flannels saturated with the tincture may be applied to the abdomen, or poultices of the leaves may be similarly used. Dr. Lente (*Psychol. and Med. Leg. Journ.*, 1875) says that he has been accustomed to use, even in children, four ounces of the best English leaves, and with a quart of water "make a poultice which extends all round the body, and from the thorax to the pelvis." Only in desperate cases is such heroic use of the remedy warrantable. Dr. E. F. Fannell has seen (*British Med. Journ.*, March 11, 1871) almost fatal collapse produced by the external use of an ounce of the tincture in a case of renal dropsy.

ADMINISTRATION.—The dose of the powder of digitalis, as a diuretic, is three grains a day (in divided doses), increased by a grain every second or third day, until some sensible effects are manifested. The infusion or the tincture may be substituted for the powder, in corresponding dose. Digitalis, in the majority of cases, is best given in combination: in cardiac dropsy it is much more efficient if given with squill; in renal diseases the bitartrate of potassium may be exhibited simultaneously. Whilst our present knowledge of the physiological action of digitalis is in accord with the ascertained clinical fact that it is safe to give the drug cautiously in the last stages of cardiac exhaustion, yet it should never be forgotten that, as a diuretic, digitalis sometimes refuses to act, and that it is possible to produce the most profound depression with it without inducing the desired result. It is, therefore, worse than useless to persist with the medicine to the danger of the patient after its constitutional effects have been distinctly produced and no diuresis has occurred. The diuretic *external* use of digitalis is made by putting a poultice of an ounce of the fresh leaves upon the abdomen of the patient, or, preferably, flannel cloths wrung out of the infusion may be applied to the same part and covered with oiled silk, or half an ounce to an ounce of the tincture may be sprinkled upon previously-moistened spongiopiline. In either case the application should not be allowed to stay on for more than eight hours, at the expiration of which period it should be removed, to be replaced at the end of six hours if no effect has been produced.

SCOPARIUS, U. S.—*Broom* is the dried tops of Cytisus Scoparius, or the common broom-plant of Europe, cultivated in, and in some places escaped from, the gardens in this country. The drug occurs as greenish pentangular twigs with minute downy leaves, having a bitter nauseous taste, and, when bruised, a peculiar odor. Two principles have been discovered by Dr. Stenhouse in scoparius, *Scoparin*, a neutral crystallizable body, to which, he believes, the drug owes its diuretic properties, and a liquid alkaloid, *Spartein.* This alkaloid appears to influence the nervous system; although the testimony concerning it is discordant. According to Husemann (*Die Pflanzenstoffe*, p. 64), Mitchell found that about four grains of it administered to a rabbit caused death in three hours, preceded by a very short stage of excitation and then deep sleep without convulsions, whilst in Schroff's experiment a single drop caused in the rabbit violent convulsions, followed by a stage of muscular weakness, depression of the heart's action, renewed convulsions, and finally death. In an elaborate examination of the action of large doses of spartein (*Archiv für Exper. Path. u. Therap.*, 1873), Dr. Fick arrives at the following conclusions as to the influence of poisonous doses of spartein: 1. So far as can be ascertained, spartein affects the intellectual functions both of frogs and of the mammalia, and can therefore to a certain extent be regarded as a narcotic. But this effect upon the brain is not a very marked one in degree, since, even in cases where the most decidedly poisonous results have been produced, entire suspension of consciousness has not been observed. 2. Spartein exhibits powerful toxic effects upon the spinal cord, the reflex action of which in particular is lessened to a great degree. 3. Spartein paralyzes the motor nerves, which after a larger dose of the poison lose their electrical excitability entirely. 4. A small dose of spartein causes the suspension of the electrical excitability of the vagus, so that its excitation produces no interfering influence on the motions of the heart. In larger doses the governing centres themselves are paralyzed, so that neither by the use of muscarin nor by other means can a diastolic cessation of the heart be produced. 5. In the poisoning of mammalia by spartein, death is dependent upon paralysis of the respiratory centres. By employing artificial respiration, life may be prolonged in the poisoned animals for some time.

In very large doses, scoparius produces in man free purging, and even vomiting; but as ordinarily used it is simply a most efficient hydragogue diuretic. It is very largely used in general *dropsy*, and is one of the most reliable remedies of the class, seldom failing unless the structural lesions are such as to prevent any diuretic from acting. It is best given in decoction: half an ounce of the tops in a pint of water boiled down to half a pint. Of this an ounce may be given every three hours until some effect is produced; or a fluid extract, which is not officinal, may be given in half-drachm doses.

SPIRITUS ÆTHERIS NITROSI, U. S.—*Sweet Spirit of Nitre* will be considered in the class Diaphoretics, in detail. Suffice it for the present to state that when given in a single large dose (a teaspoonful to a tablespoonful) and the patient afterwards kept cool, sweet spirit of nitre acts as a pretty efficient diuretic, increasing the watery portion of the urine, but not to such an extent as to render the drug available for use by itself in dropsy. It acts upon the kidneys as a mild, soothing stimulant, and is mostly employed as an adjuvant to more powerful diuretics, or by itself when there is simply diminished renal excretion of functional origin, or when the kidneys suffer from slight congestion, as shown by aching in the loins without other more serious symptoms.

REFRIGERANT DIURETICS.

POTASSIUM. (K.)

The salts of potassium, like the substance itself, are very poisonous to the lower animals. According to Dr. Paul Guttmann, they are all exactly alike in the character and the intensity of their action; but further experimentation is wanting before this point can be considered as decided, and I have preferred to study the bromide entirely separate from its congeners.

In the experiments of Podocaepow (*Virchow's Archiv*, 1866, Bd. xxxv. p. 460) it was found that one cubic centimetre of a solution of the chloride (one to five), given to a frog by the stomach, would in eight minutes cause abolition both of voluntary and of reflex movements. After from fifteen to twenty minutes, cardiac arrest occurred. Upon mammals similar results were obtained, but the abolition of motility was apparently not so profound as in the frog. Thus, four or five drachms of the chloride of potassium injected into the stomach of the dog caused bloody stools, reduction of temperature, muscular weakness, and death without convulsions. Although in most, if not all, of the reported cases of poisoning by potash salts, the most prominent symptoms are those due to the local action upon the alimentary canal, yet it would seem that poisonous doses act upon man as upon other mammals, as great feebleness of pulse and lowering of temperature have been noted as constant phenomena.

Circulation.—The most marked action of the potash salts is upon the heart. When a frog is killed by a salt of potash, the heart* is arrested in diastole, according to both Podocaepow† and Guttmann. The blood-current before death is greatly lessened in force, as was determined by Podocaepow by watching the circulation in the web, and by comparative experiments in regard to the rate at which blood flowed from wounded vessels in poisoned and in unpoisoned frogs. In mammals, potash influences the heart even more markedly than in cold-blooded animals. Ten or fifteen grains of the chloride quickly injected into the jugular vein suffice to produce instant cardiac death. According to Aubert and Dehn (*Pflüger's Archiv*, 1874, p. 122) for a few seconds before complete suspension of movement there are irregular, "stormy" convulsions, which run through the heart in a sort of peristaltic manner with great rapidity, but have no effect in expelling the blood. A curious fact discovered by Aubert and Dehn is, that the effect of the potash is not permanent unless it has continued a certain length of time. Thus, a hound received into its jugular a fatal dose of the chloride of potassium, and ten seconds after all pulsations had ceased the crural artery of a second dog was connected with the jugular of the poisoned animal, when the heart recommenced its movements, only to cease again after a time. The action of a poisonous dose of potash upon the heart appears to be a local one. Traube found that when death in the dog was produced by injection into the jugular the heart-muscle failed entirely to respond to electricity. In this case, however, the heart received at once the full dose of the poison, and the careful experiments of Podocaepow and of Guttmann have shown that when the potash is introduced gradually and in the more ordinary methods into the circulation, the contractility of the cardiac muscle, although very much impaired, is not at the time of death entirely destroyed; in frogs it is less affected than in warm-blooded animals. Guttmann has found that previous section of the vagi has no influence upon the action of large doses of potash. The diastolic arrest is therefore independent of the inhibitory system, and is due to a direct impression upon the cardiac muscle.

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* The poisonous influence of potash upon the heart was, I believe, first discovered by Black (*Comptes-Rendus*, 1839), and has been confirmed by Bouchardat (*Annuaire de Thérapeutique*, 1844), by Grandeau (Robin's *Journal de l'Anatomie*, 1864), by Rabuteau, (*L'Union Médicale*, 1871), and by others.

† *Virchow's Archiv*, Bd. xxiii. It is proper to mention that Podocaepow states, on p. 506, that the arrest is sometimes systolic, sometimes diastolic, although on p. 511 he asserts that the arrest never occurs in systole.

Although the effects of large doses of compounds of potassium on the heart appear to be made out, definite knowledge is still wanting in regard to small doses. Traube (*Gesammelte Beiträge*, Bd. i. p. 386) asserts as the result of his experiments that, injected into the blood in doses of two or three grains, the nitrate of potassium produces a fall in the pulse and a rise in the arterial pressure. Aubert and Dehn (*Pflüger's Archiv*, 1874, p. 126) have experimented with a number of the salts of potash, and found that, with the exception of the permanganate, they all act upon the circulation in the manner just described. If larger doses of the potash preparations were employed, the rise was preceded by a temporary fall of pressure, and if the dose were still larger, the fall was permanent. The first fall of pressure, as well as the permanent impression produced by large doses, was probably caused by the direct action of the drug upon the heart-muscle. The cause of the rise is still enveloped in obscurity, as is also the manner in which potash affects the pulse-rate. Traube affirms that if the vagi be cut after exhibition of the potash salt, the lessened pulse-rate instantly becomes rapid, and the already increased arterial pressure rises still further. The same observer also found that after section of the pneumogastrics small doses of the nitrate produced a fall in the pulse, with increased arterial pressure; but on a repetition of the dose in the same animal no lessening of the pulse-frequency was perceptible, while each time the pressure rose. This seems to indicate that the cardiac action of the drug is independent of the inhibitory apparatus, which is confirmed by the experiments of Aubert and Dehn (*loc. cit.*, p. 145) upon atropinized dogs. It is very probable, but not in any way proven, that the rise of pressure is brought about through the vaso-motor nerves. Both Podocaepow (*loc. cit.*, p. 515) and Aubert and Dehn (*loc. cit.*, p. 150) have called attention to the very temporary effect of the potash injections: thus, after small doses the arterial pressure returns to its normal position in three minutes; after large doses the maximum effect is reached in ten minutes. Aubert and Dehn also assert that there is no cumulative action, many small doses given at brief intervals leaving no residual effect; but this is in direct opposition to the statements of Guttmann. Köhler affirms that after section of the spinal cord potash salts have less influence upon the heart, and that larger doses are required to kill (*Centralb. Med. Wiss.*, 1877, p. 675). The only fixed conclusion warranted by the evidence is the absolute necessity of further investigation.

Muscular and Nervous Systems.—The action of the drug upon the motor system is more marked in cold- than in warm-blooded animals. Podocaepow believes, but does not definitively prove, the paralysis of both voluntary and reflex movement to be of muscular origin. The much more elaborate experiments of Guttmann show that the muscles of poisoned frogs are not only excitable at the time of death, but are nearly as sensitive as normal muscles, and maintain their excitability nearly as long after death. As both nerve-trunks and muscles are capable of performing their functions in the dying frog, Guttmann concludes that the paralysis is of spinal origin, a conclusion which he confirmed by tying the aorta directly above its bifurcation and then administering the potash, when the paralysis appeared as early in the protected hind legs as in the non-protected front ones.

By an elaborate series of experiments, Drs. Ringer and Murrell have shown that the potash salts, in sufficient concentration, act powerfully upon the cerebrum, the motor and sensory nerves, and the muscles; in a word, that they are poisonous to all the higher forms of tissue. In poisoning, however, the brain and spinal cord suffer in their functional activity far more quickly and deeply than do the peripheral, nervous, and muscular tissues; consequently, in general poisoning the symptoms are produced through the higher nerve-centres (*Journal of Physiology*, i. 88). All of the potash salts probably act in a similar manner* upon the spinal cord, their power, according to the experiments of Ringer and Morshead (*Journ. Anat.*, xii. 82), being in direct proportion to the amount of potash they contain.

General Influence.—Outside of the body, potash favors very greatly the oxidation of organic substances. Thus, when olein is exposed to ozone no change occurs, but if potash be added rapid oxidation follows. Again, when albumen or hæmatin is dissolved in water no change, or a very slow one, occurs, but if potash be added the organic principle is oxidized with extraordinary rapidity. Whether a similar influence is or is not exerted within the body is not as yet completely determined, but the present evidence strongly indicates that it is.† The fall of temperature produced by poisonous doses of potassium salts would seem to point to lessened oxidation, but is probably simply the result of the profound depression of the circulation. The chief arguments in favor of the theory of increased oxidation in the system as yet brought forward have been drawn from studies of the action of the drug upon the urinary excretion in health and in disease. Potash or its salts administered in sufficient quantity certainly, under ordinary circumstances, increase the watery portion of the urine; but, as Prof. E. A. Parkes and others have demonstrated, they do more. In an elaborate series of experiments upon himself, Prof. Parkes found (*Brit. and For. Med.-Chir. Rev.*, 1853, xi. 258) that liquor potassæ (f℥ii) when taken fasting produced in from thirty to ninety minutes an increased flow of slightly acid urine containing the whole of the alkali and organic matter, which differed in quality from that ordinarily found in urine, and was also larger in amount than normal. An organic acid, certainly neither uric nor hippuric, was believed to form a part of the solid matter by

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* Ringer and Murrell, applying the chlorides, iodides, and bromides of potassium and ammonium directly to the ends of the afferent nerves, found that they paralyzed, the effect of the potash salt being much the most powerful and permanent, that of ammonium the next, and that of sodium the least (*Journ. Anat.*, xii. 71).

† Lehman was, I believe, the first to originate the oxidation theory.

Parkes, who attributes the alteration of the urinary solids to the oxidizing influence of the potash. Taken after meals, the liquor potassæ acted simply as an antacid, and had no perceptible effect upon the urine. Both the acetate and the nitrate of potash in Parkes's experiments failed to act on the urine, probably because taken in too small doses, for it is a fair presumption that their oxidizing influence is less than that of potash itself. Certainly other experimenters have found that they do influence the urinary excretion. Golding Bird found (*On Urinary Deposits*, 2d Amer. ed., 1859, p. 356) that in a case carefully tested, under favorable circumstances, three drachms of the acetate of potassium increased the solids of a dog's urine from four hundred and sixteen to seven hundred and eighty-two grains, or, deducting all the eliminated potash, to over six hundred grains. The increase of the uric acid was about thirty-two per cent.; of the urea, about sixty per cent.; of extractives, including creatine, creatinine, etc., about twenty per cent.; or, speaking absolutely, the uric acid was increased eighty-five grains, the urea seventy-two grains, and the extractive, thirty-six grains. Rabuteau (*L'Union Médicale*, 1871, p. 389) found that the daily ingestion of seventy-five grains of the chloride of potassium caused an increase of twenty per cent. in the amount of urea discharged. Aug. Dehn has also experimentally found that the potash salts greatly increase the elimination of urea (*Pflüger's Arch.*, Bd. xiii. p. 368).

The various studies which have been made as to the action of the potash salts in disease seem to bear out the oxidation theory. In six observations upon subjects affected with what may be termed indifferent diseases, such as lead-palsy, Parkes (*Brit. and For. Med.-Chir. Rev.*, xiv., 1854) found that the urea was increased, and also the sulphuric acid, by the use of drachm doses of liquor potassæ. Dr. Austin Flint (*American Med. Monthly*, Oct. 1860) has studied the effect of the nitrate of potassium upon a number of persons suffering from various diseases, and found that it very greatly increases the amount of solids in the urine. In rheumatism Prof. Parkes found that the liquor potassæ increased the elimination of sulphuric acid, but had no decided influence on the uric acid. He, however, used such small doses of the drug as not to get the effect obtained in the alkaline treatment of the disease, since he expressly states that the urine remained acid (*Brit. and For. Med.-Chir. Rev.*, 1854). Rheumatism, gout, and the uric acid diathesis certainly bear some relation with one another. It has long been customary to use potash salts in excess of uric acid in the urine, and the relief obtained has been believed to be due to the conversion of the acid into a urate. Dr. Basham affirms (*Practitioner*, vol. v., 1870), however, that as the result of a series of analyses he has found that in uric acid diathesis not only is there a great increase of the urea during the use of potash, but that the uric acid, either free or combined, in the urine is greatly diminished. Dr. Basham, remembering that Mr. Schunck had proved that, under the oxidizing power of potash, uric acid outside of the body is converted into oxaluric acid, which in its turn is readily metamorphosed into oxalic acid and urea, carefully examined the urine of gouty patients taking the potash, and found that not only was the urea increased, but that oxalic acid also appeared as the uric acid decreased, and that the urine, on standing, deposited crystals of oxalate of calcium, although none of those could be found in it when first voided. This research of Dr. Basham certainly seems to demonstrate that in uric acid diathesis the potash salt increases the oxidation and the ultimate metamorphosis of tissue. Where this occurs, whether in the blood, in the kidney, or in the urine itself, is not at present determined.

Rabuteau, in his experiments with the chloride, found that the urine maintained its acidity. It is notorious, however, that large doses of the acetate, carbonate, or citrate of potassium produce alkalinity of the urine. The explanation of the apparent contradiction is that the vegetable salts are destroyed in the system and eliminated as alkaline carbonates, whilst the nitrate, and probably chloride, sulphate, and similar compounds, pass entirely, or in great part, unchanged through the body. A proof of the latter fact is furnished by Prof. Alfred S. Taylor (*Guy's Hospital Reports*, 1863, p. 177), who from the urine of a patient taking two hundred and seventy grains of the nitrate daily, obtained 158.7 grains of the ingested salt per diem. A portion of the potash salts escapes through the intestines, as Dr. Kramer (*Annales d'Hygiène Publique et de Médecine Légale*, vol. i., 1843) has found the nitrate in the fæces of animals taking it; and it is much more probable that the nitrate not accounted for in Dr. Taylor's investigation was eliminated by the intestines than that it was decomposed in the system. If, as there is much reason to believe, a vegetable acid when given alone passes through the system in great measure unchanged, whilst, as asserted by Dr. Münch (*Archiv des Vereins für gemein. Arbeiten*, 1863, p. 370), and as seems to follow from the facts already brought forward, the same acid is found when combined with an alkali to be destroyed by oxidation, there is in this strong corroboration of the belief that the alkalies aid oxidation in the system. Putting all the evidence together, it seems to me that the oxidation theory must be accepted as exceedingly plausible and probable, although not, perhaps, absolutely proven.

When a potassium salt is given in large doses for a long time, it produces a condition of dyscrasia, with impoverishment and excessive fluidity of the blood. How or why it has this action is unknown, as indeed is the exact nature of the changes. Very probably there is some connection between these changes and the oxidizing power of the drug; but any theory in the present imperfect state of our knowledge could at best be only an ingenious speculation.

Our knowledge of the physiological action of the potassium salts seems to show that the vegetable salts and the carbonates are equivalents, but that the mineral salts are more or less peculiar and individual; and clinical experience confirms this. There is, however, one exception: the bitartrate of potassium appears to act differently from the other vegetable acid salts, and, although direct proof is wanting, probably is not decomposed in the system. Potash itself is never used to affect the system, on account of its irritant properties; and its local action will be discussed under the headings of Escharotics and Antacids. I shall here group all the potassium vegetable salts, except the bitartrate, together.

POTASSII CARBONAS.

The potash of commerce, obtained from wood-ashes and other sources, occurs in the form of fused, stony masses, variegated in color, and of a caustic, burning taste; when purified so as to form *pearlash*, it becomes of a bluish-white color. When further purified so as to conform with the officinal tests, it occurs as a coarse, granular, whitish powder, very deliquescent, soluble in its weight of water, insoluble in alcohol. It should contain only traces of the sulphate, chloride, and silicate of potassium.

POTASSII BICARBONAS, U. S.—*Bicarbonate of Potassium* is manufactured by passing carbonic acid gas through a solution of the carbonate in distilled water. It occurs in transparent, colorless crystals, not deliquescent, slightly alkaline to the taste and to test-paper. It dissolves in four times its weight of boiling water, but is insoluble in alcohol.

Therapeutically the carbonate and bicarbonate are of equal value, except that the carbonate is more irritant, and is therefore not so well borne by the stomach as is the bicarbonate. On account of its nauseous taste, even the latter salt is not so available as the acetate or the citrate. The full dose of the bicarbonate is half an ounce daily, given in diluted solution.

POTASSII CITRAS, U. S.—*Citrate of Potassium* is a whitish, granular, deliquescent salt, of neutral or very slightly acid reaction, freely soluble in water. It is the least offensive to the palate of all the potash salts, except the tartrates. *The Solution of Citrate of Potassium* (*Liquor Potassii Citratis*, U. S.,—Bicarbonate of Potassium, 960 grs.; Citric Acid, 720 grs.; Water, 24 f℥), and the *Neutral Mixture* (*Mistura Potassii Citratis*, U. S.,—Lemon-juice, Oj; Bicarbonate of Potassium, enough to neutralize), have been long used as diaphoretics in sthenic fevers. The dose is half a fluidounce to one fluidounce every one or two hours. A very elegant method of exhibiting neutral mixture is in the form of *Effervescing Draught*. It is especially useful when there is any tendency to sick stomach. It should be prepared in two solutions: one consisting of lemon-juice and water, equal parts, or of citric acid ʒii, water f℥iv; the other of bicarbonate of potassium ʒi, water f℥iii. An ounce of each of the solutions to be put together, and the whole to be drunk during effervescence.

POTASSII ACETAS, U. S.—*Acetate of Potassium* is a perfectly neutral white salt, of a decidedly saline taste, extremely deliquescent, and soluble in half its weight of water. It is made by dissolving the bicarbonate in acetic acid, and evaporating. It occurs sometimes as soft, fibrous masses, at other times it has a foliated structure.

THERAPEUTICS.—An important use of the vegetable salts of potassium is in *acute inflammatory rheumatism.* Before the introduction of the salicylates the alkaline treatment was the best that was known for cases of thoroughly acute rheumatism: the medicine must be given freely, an ounce to an ounce and a half in the day, and be persisted in, opium, of course, being at the same time employed in as large doses as is necessary to relieve the pain; after a few days, when the violence of the symptoms has abated and decided anæmia appears, the exhibition of the drug should be discontinued and iodide of potassium, with tonics, be substituted. In cases subacute from the beginning I have found a combination of the iodide and acetate of potassium very efficient, ten grains of the former and thirty of the latter being administered three or four times a day. The potash probably does good in rheumatism by lowering arterial action, by favoring oxidation and elimination of partially effete materials, and by neutralizing excessive acidity. Be the method what it may, I have no doubt of the great clinical value of the remedy, its applicability being in direct proportion to the acuteness and violence of the symptoms.

As depuratives, the potash salts are very useful in various diseases. Attention has been especially called by Dr. Golding Bird to their value in that class of cases spoken of as "*chronic biliousness;*" in chronic *malarial poisoning*, in *catarrhal jaundice*, and in the *jaundice* of simple *hepatic torpor*, they are often of use. In *uric acid gravel* and in *uric acid calculus* there can be no doubt of the value of potash as a prophylactic, as a preventive of the formation or deposition of the uric acid. The remedy has also been used to dissolve uric acid *calculi;* but the results offer such slight encouragement that it is only necessary here to give a reference to the work of Dr. Wm. Roberts (*On Urinary and Renal Diseases*, Am. ed., 1866).

ADMINISTRATION.—As usually exhibited, the potash salts are exceedingly distasteful. There is no need of this whatever. The citrate may be given dissolved in lemon-juice, or, what is a still more pleasant method, a syrupy solution of the bicarbonate and the citrate may be made, of such a strength that every tablespoonful of it shall contain half a drachm of each salt. At the time of exhibition one or two tablespoonfuls of this may be put in a little water, and to it be added a large tablespoonful of lemon-juice, the whole to be drunk whilst effervescing. If the patient takes in the course of the day six of the largest doses mentioned, the whole amounts to an ounce and a half of the citrate of potassium. When the remedy is used simply as a depurative, as in jaundice, such large doses are, of course, not proper; a teaspoonful of the alkaline solution, with a corresponding amount of lemon-juice, taken three times a day, will generally be sufficient.

POTASSII BITARTRAS, U. S.—*Bitartrate of Potassium*, made from argol (see Tartaric Acid), occurs in white crystalline crusts or masses, which are commonly pulverized before being sold as *Cream of Tartar*. It usually contains tartrate of calcium, and is only sparingly soluble in cold water. It appears to differ therapeutically from its congeners in being more actively diuretic, and in acting more powerfully as a hydragogue cathartic. Half an ounce to an ounce of it given at once will very generally cause watery purging. In this city it is probably employed more frequently in *dropsy* than any other diuretic: the usual plan is to dissolve an ounce of it in a pint of infusion of juniper-berries, and have this all taken, in divided doses, during the twenty-four hours. In acute *desquamative nephritis*, cream of tartar is a very useful diuretic: as, however, the avoidance of irritation of the kidneys is imperative in this disease, the alkaline diuretic should not be administered in infusion of juniper.

The *Tartrate of Potassium* (POTASSII TARTRAS, U. S.) is rarely used in medicine. It is said to be actively purgative in doses of half an ounce.

POTASSII SULPHAS, U. S.—*Sulphate of Potassium* occurs in small, aggregated, transparent, very hard crystals, permanent in the air, usually short six-sided prisms, possessing a nauseous somewhat bitter taste. It is insoluble in alcohol, slowly soluble in nine and a half times its weight of cold and in less than four times its weight of boiling water. Sulphate of potassium is said to be "a mild purgative, operating usually without heat or pain or other symptoms of irritation," in doses of four or five drachms; and in doses of one or two drachms acting as a laxative. It is, however, very rarely employed in this country as a purgative. Sulphate of potassium, in doses not a great deal in excess of those which have been recommended by practitioners, acts as an irritant. Dr. Mowbray states that the salt is used in France as a popular abortifacient, and that he has seen very alarming symptoms produced by four drachms of it. Dr. Taylor records a case in which less than two ounces caused in a woman severe vomiting, purging, abdominal pain, and finally death. At the post-mortem the stomach and intestines showed very decided evidences of inflammation.

POTASSII NITRAS—NITRATE OF POTASSIUM. U.S.

Nitrate of Potassium, or *Nitre*, is either obtained from certain saline earths, occurring chiefly in India, but to a certain extent in other portions of the world, or else is artificially manufactured in nitre-beds formed out of animal and vegetable matter, wood-ashes, and calcareous earth, or, finally, is obtained from old plaster rubbish. In the "nitre-beds," as well as in the natural saline earths, which have undoubtedly in the beginning contained animal and vegetable matters in a state of decomposition, nitric acid is formed by the oxidation of ammonia, and unites with the bases in the soil. Most of the nitre used in this country comes from Calcutta, through Boston, packed in grass-cloth bags. *Chili saltpetre* is the *nitrate of sodium*, which impregnates certain soils in the country whose name it bears. It is undoubtedly formed in these soils by a process precisely analogous to that in which the nitre of India is produced, excepting that, little or no vegetable matter being present to afford the potassium during the decomposition of the animal matter and the generation of nitric acid, the latter unites with the calcium of the soil. Chili saltpetre is employed as a substitute for true saltpetre in the manufacture of nitric acid, and may be made into the nitrate of potassium by means of crude potash.

Saltpetre occurs in more or less perfect, long, striated, semi-transparent, six-sided prisms, with dihedral summits; of a sharp, saline, somewhat cooling taste; containing no water of crystallization, but decrepitating when thrown on the fire, from the evaporation of water mechanically retained in the crevices of the crystals; soluble in four or five times their weight of cold and in two-fifths of their weight of boiling water, sparingly soluble in proof spirit, insoluble in absolute alcohol. At a high heat they decompose, liberating a large quantity of nascent oxygen, and thereby greatly intensifying the combustion of surrounding objects. The *Sal prunelle* of the shops is a saltpetre which has been fused and run into circular moulds.

PHYSIOLOGICAL ACTION.—Nitrate of potassium applied to any raw surface, or to a mucous membrane, acts as a violent irritant. As death has not infrequently resulted from its ingestion, whilst it has occurred very rarely from that of any of the other ordinary salts of the alkali, it has generally been thought that nitre possesses peculiar properties. It is not to be gainsaid, however, that the cause of death in nitre-poisoning is very generally the local inflammation of the stomach and intestines produced by it,—effects dependent simply upon its irritant properties, and not upon any constitutional action; a conclusion becoming doubly evident when it is remembered that, if the drug be given in weak solution, much larger amounts can be exhibited with only therapeutic effects than would cause death if administered in solid form or in very concentrated solution. Thus, in a case under the care of Dr. Wilks (*Guy's Hosp. Rep.*, vol. ii., 3d series, 1863, p. 173), a man suffering from renal dropsy took, between October 28 and December 26, 1862, one pound twelve ounces and six drachms of the nitrate of potassium, with benefit. As one ounce has caused death in three hours (Taylor, *Principles and Pract. of Med. Jurisp.*, 2d ed., vol. i. p. 237), this patient received in fifty-nine days the equivalent of twenty-eight fatal doses. Again, according to Prof. Stillé (*Therapeutics*, vol. ii.), Dr. Brocklesby habitually prescribed one ounce of the salt a day, and Dr. Martin-Solon even two ounces per diem.

The symptoms of poisoning by the nitrate of potassium are pretty constant, and yet, as in other irritant poisoning, vary within certain limits. Very generally there is first an intense burning pain in the stomach, coming on in a few minutes after the ingestion of the poison, and soon followed by violent vomiting, and, it may be, free purging. In a little while collapse develops, with great muscular weakness, not rarely with local convulsive tremblings. The matters vomited, and even the stools, may be bloody (case, Th. Husemann, *Journal für Pharmacodynamik*, 1859, ii. 178). Sometimes the nervous symptoms predominate, and the purging may be absent; collapse, with slight vomiting and with or without paralysis of the lower limbs, may alone exist. Suppression of urine has been noted in some cases (case, *Pharmaceut. Journ.*, Feb. 1846, p. 356). After death, very grave lesions are found in the stomach and the intestines, such as intense redness and congestion, effusion of blood into the submucous coat, and sometimes into the stomach itself. Even ulceration and corrosion of the mucous membrane nave been observed. It is evident that the symptoms previously detailed as existing during life are in accord with the post-mortem results, and all point to the irritant action of the drug as the source of trouble. The predominance of the nervous symptoms in some cases is no more than is exceptionally seen in other forms of irritant poisoning (see Antimony), and is no proof of a special action of the drug upon the nervous system. Sometimes, however, death has occurred, in poisoning by saltpetre, with great suddenness. In the only cases of this character the record of which I have met with, the dose has been very large, and it is possible that the death was the result of the action of the drug upon the heart, for, like the other salts of potash, it has a direct paralyzing influence upon the cardiac muscle.

Nitre has been supposed by practitioners to be especially sedative to the circulation; but there is no reason to believe that it is any more powerful as a cardiac sedative than the vegetable salts of the base. It certainly shares the diuretic properties of the latter, but appears to be more irritant to the kidneys, since it seems difficult otherwise to account for the suppression of urine already noted as occurring occasionally in poisoning by it. It is possible that nitre may differ to some extent in its actions from the other salts of potash, on account of its acting upon the blood as a nitrate. (See page 334.)

THERAPEUTICS.—Nitrate of potassium has been especially used in *acute rheumatism*, and when given in large doses has some favorable influence upon the course of the affection. It is certainly, however, a more dangerous remedy than the vegetable salts of the base, and, according to my experience, much less efficacious. I can therefore see no good reason for continuing the practice. If given, not less than an ounce should be dissolved in a full *quart* of barley-water or other demulcent, and be administered in divided doses during the twenty-four hours.

In the treatment of poisoning by saltpetre, after the stomach and bowels have been emptied, the usual means for the relief of toxic gastro-enteritis should be resorted to.

POTASSII CHLORAS. U.S.—CHLORATE OF POTASSIUM.

This salt is said to be chiefly prepared by heating the solutions of the hypochlorite of lime and chloride of potassium; on cooling, the chlorate of potassium crystallizing out and the chloride of calcium remaining in solution. Chlorate of potassium occurs in white rhomboidal plates of a pearly lustre, of an acerb taste, dissolving in sixteen parts of water at 60° F., and in two and a half parts of boiling water.

Physiological Action.—Upon mucous membranes and ulcerated surfaces this salt acts as a powerful irritant, being, I think, even more active in this respect than the nitrate of potassium. Taken internally in sufficient quantities it is a powerful poison, and has frequently caused death. There are on record a large number of fatal cases, most of which are collected in the brochure of Dr. J. von Mering (*Chlorsaure Kali*, Berlin, 1885). To Dr. Jacobi, of New York, belongs the credit of having first called attention to the dangerous action of this much-used remedy (*American Med. Times*, April, 1861, p. 245). The smallest amount which will produce death is not known, but in a case recorded by Dr. Matthisson, a little over half an ounce taken in the course of several days proved fatal. A drachm in the course of a night has killed an infant of a year old, and three drachms, a child three to four years old. In most cases of fatal poisoning in the adult the dose has been much over half an ounce. The symptoms may be acute or subacute. In the rapid cases there have been violent vomiting, profuse diarrhœa, excessive dyspnœa, great failure of the heart's action, and marked cyanosis. In most of these cases the blood has been found of a chocolate color. In the subacute cases the gastro-intestinal symptoms have been severe with generally vomiting of blackish-green matters, and distinct swelling of the liver and the spleen. The urine is markedly lessened in quantity, albuminous, often of an opaque reddish-brown or blackish color, showing under the microscope brownish or yellowish-brown tube-casts, often containing the detritus of blood-corpuscles. Hæmiglobinuria has been noticed (*Trans. Internat. Congress*, 1881, vol. l. p. 463), and methæmoglobin is a common constituent. The nervous symptoms have been severe delirium, coma, tonic and chronic cramps, and a peculiar stiffness of the extremities.

Headache, loss of appetite, violent pains in the abdomen and other portions of the body, and marked abdominal tenderness have usually preceded the loss of consciousness. Not rarely upon the surface of the body are there minute small ecchymoses, and even more frequently there is a general jaundice. In some cases the patient has rallied and seemed to be on the road to recovery when the fatal relapse has occurred.

After death the blood is usually chocolate-colored, the gastro-intestinal tract inflamed, the liver and spleen are enlarged and filled with the brownish débris of red blood-corpuscles; the bone-marrow and the brain are often similarly colored, whilst the mucous membranes are usually swollen and ecchymosed. The kidneys are profoundly affected, their tubules full of brownish casts and their epithelial structure evincing a nephritis. The most characteristic and probably the most important of the lesions is the change in the blood, which was first noticed after death by Felix Marchand (*Virchow's Archiv*, Bd. 77, 1879). Dr. L. Riess (*Berlin. Klinisch. Wochenschrift*, 1882) noted in a case during life that many of the red blood-corpuscles were decolorized, and others contained little granules of an elliptic shape. The researches of Marchand, abundantly confirmed by subsequent investigators, show that the changes in the blood are the result of the formation of a substance apparently identical with the methæmoglobin of Hoppe-Seiler and characterized by the appearance in its spectrum of a blackish line in the red. The same substance is readily produced by mixing either the chlorate of sodium or the chlorate of potassium with human or animal blood outside of the body.

It was asserted years ago by Dr. Stevens that when the chlorate of potassium is taken internally the venous blood acquires an arterial hue, and the confirmatory statements of Dr. O'Shaughnessy led many of the profession to give credence to the idea that the chlorate yields its oxygen to the blood; so that it has been used to an enormous extent in various low forms of disease with the idea of increasing oxidation in the blood. It is beyond cavil that the observers just quoted mistook the altered coloration of the blood for the arterial hue. It is very improbable from a chemical stand-point that chlorate of potassium should part with its oxygen in the blood at the temperature of the body, and there is no proof that it does so. It has been shown by Rabuteau and other observers that the chlorate of potassium escapes unchanged with the saliva, urine, and probably all the secretions of the body. Isambert found it in the tears, the bile, the nasal mucus, and even in the milk of nursing women. Rabuteau took five grammes of the salt, and recovered from the urine 4.873 grammes (*Gazette de Méd. de Paris*, p. 30). Isambert, in two experiments, recovered respectively ninety-five and ninety-nine per cent. of the ingested chlorate of potassium from the urine. J. von Mering, out of fifteen grammes given to a dog, obtained 14.7 grammes; out of five grammes which he took himself, 4.62 grammes, and when he took but a single gramme he recovered in the urine of the next ten hours 0.91 gramme. From the saliva and urine of a case of mercurial stomatitis in which five grammes had been exhibited he recovered 4.54 grammes. When the escape of the salt through other channels than the kidneys is remembered, these experiments appear to prove it is possible to recover practically all of the ingested chlorate, and that it all escapes unchanged from the body. F. von Mering, however, believes that some of the chlorate of potassium is reduced in the system, chiefly because he thinks that methemæglobin is formed by a process of oxygenation. The exact nature of methæmaglobin is, however, not made out: according to C. A. Macmunn (*Spectroscope in Medicine*, p. 100, 1881), methæmaglobin is probably a mixture of hæmatin with soluble albumen, as it has been shown by Hoppe-Seiler that it is not formed by oxidation. M. von Mering in one or two instances in the dog found a slight increase in the chlorides of the urine during the administration of the chlorate, and it is possible that a minute quantity of the chlorate does undergo deoxidation, but it must be considered established that any such change affects so small a portion of the drug as not to be worthy of consideration.

The effect of therapeutic doses of chlorate of potassium upon the system is certainly not marked, and is probably the same as that of the nitrate. The potash seems to exert some influence, as Isambert states that the drug directly injected into the jugular vein paralyzes the heart, and produces a general depression similar to that caused by the nitrate. In his experiments upon himself, Isambert found that when taken in large doses, two to five drachms a day, the chlorate caused salivation, free diuresis, increase of the appetite, and when not well diluted, gastric irritation; the urine continued strongly acid, and contained an excess of rosacic acid, uric acid, and the urates.

THERAPEUTICS.—The chlorate of potassium has been very freely used, and with great asserted advantage, in all forms of disease believed to be due to blood-poisoning: such as *scarlet* and other *adynamic fevers*, *diphtheria*, *scorbutus*, *syphilis*, and even *hydrophobia*. As already stated, the theory upon which this practice rests has no foundation in reason or science, and my own empirical experience with the remedy has been in exact accord with the teachings of physiology. I have seen the chlorate repeatedly employed in various diseases of the class just spoken of, and have never seen it do a particle of good. On the other hand, in various forms of *stomatitis* the remedy is undoubtedly of great value. Thus, there is a great deal of evidence of its usefulness in mercurial sore mouth; and when given in the form of a powder, with sugar, it almost always acts like a charm in the *follicular* or *aphthous stomatitis* of children.* I do not believe, however, that its influence in these cases is other than local; yet, as the remedy is eliminated with the saliva, and, therefore, when given internally is constantly present in the mouth, the ordinary method of using it is probably the best. The salt now under consideration has been used in *ascites* and other *dropsical* affections, but is, undoubtedly, inferior to the other salts of the alkali. When used *locally*, the chlorate of potassium acts as a stimulant to the various mucous membranes, and is often of excellent service in cases of *angina*, and is even said to have been used advantageously by enemata in *dysentery* and in *cholera infantum*. The most generally efficient gargle that

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* M. Laborde (*Bull. Gén. Thérap.*, lxxxvii. 1874) and M. Tacke (*Inaug. Diss.*, Bonn, 1878) have shown that the *chlorate of sodium* acts physiologically like the potassium salt; and Dr. S. Ringer and H. Sainsbury (*London Lancet*, ii., 1882, 736) have found it equally efficient in stomatitis.

I know of in ordinary *sore throat* may be made by pouring a pint of boiling water over a powder composed of an ounce of *sumach berries* and half an ounce of the chlorate of potassium, allowing to simmer in an earthen vessel, with occasional stirring, to three-fourths of a pint, straining, and using in the ordinary manner, or the fluid extract may be used (see *Rhus Glabra*, p. 32). A half-ounce to an ounce of the saturated solution of the chlorate combined with a few drops of laudanum injected into the rectum once or twice a day and retained, is often of the utmost service in *hemorrhoids*.

ADMINISTRATION.—For manifest reasons, when taken in large doses the chlorate of potassium must be exhibited in dilute solution. The usual dose is from ten to thirty grains; as a lotion, from ten grains to half a drachm may be dissolved in the ounce of water.

LITHII CARBONAS, U. S.—*Carbonate of Lithium* is a white powder, sparingly soluble in water, and readily distinguishable by the carmine-red color which it imparts to the flame of alcohol. From it the U. S. Pharmacopœia directs that the *citrate* (a white, deliquescent, freely soluble powder) shall be prepared by solution with citric acid in water. The combining number of lithia is so low that all the salts contain a very remarkable proportion of the base. We have but little accurate knowledge of the physiological action of lithia, but it probably closely resembles potash in its effects upon the system. In twenty-grain doses I have seen it apparently produce severe general prostration, amounting almost to general paralysis, in a feeble adult female, but have given it very largely to other patients without inducing any constitutional symptoms. It is eliminated by the kidneys, rendering the urine alkaline.

THERAPEUTICS.—According to the experiments of Dr. Ure and of Dr. Garrod, solutions of the lithia salts have the power of dissolving uric acid and the urates; and the drug was strongly recommended by Dr. Garrod in *uric acid diathesis* and in *chronic gout*, given in doses of three or four grains three times a day. The drug was extensively employed, but fell into disrepute until recently, when its claims have been revived, especially by Prof. Ditterich (*Schmidt's Jahrbücher*, Bd. cli. p. 270). As stated by the latter observer, it is very generally given in too large dose. In my own experience, given as prescribed by Dr. Garrod for a length of time, it has appeared to do great good in some cases of chronic gout. Either salt may be exhibited dissolved in water, in doses of five grains, three times a day; preferably taken a half-hour before eating.

BLATTA.—The dried bodies of the Blatta orientalis, or cock-roaches, have long been popularly used in Russia as a remedy for *dropsy*. Bogomolow found in them a crystalline principle which he called *Antihydropin*.* Under their influence the sweat and urine are said to be greatly increased and the dropsy rapidly to disappear. When the urine contains albumen, this is greatly lessened or disappears entirely. The proper dose is uncertain. Bogomolow (*Lond. Record*, 1877, p. 502) gives four and a half grains three times a day to children. Probably fifteen to twenty grains daily is about the proper commencing dose for the adult.

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* J. Tscherníschew (*Schmidt's Jahrb.*, Bd. cxcvii. 205) states that he has found in the cock-roach a very powerful poison, *Blattic acid*, which produces in frogs paralysis of the

STIMULATING DIURETICS.

BUCHU—BUCHU. U.S.

The leaves of the Barosma crenata, and of other species of the genus, natives of Southern Africa. These leaves, which are gathered by the Hottentots of the Cape of Good Hope, are an inch or less in length, from three to five lines broad, of various forms, but always notched on the edges, and having a strong, rather rank, yet somewhat aromatic odor, and a warm, bitterish taste. They owe their virtues, which they yield to water and to alcohol, to a volatile oil and to a bitter extractive.

THERAPEUTICS.—Owing to its bitter principle, buchu is perhaps slightly tonic; but its chief medicinal virtue is as a diuretic stimulant and alterative to the mucous membrane of the genito-urinary organs. It does not very largely increase the flow of urine, and hence is never administered in dropsy, but in all cases of subacute or chronic inflammation of the genito-urinary organs it may be employed with hope of success. Its oil is undoubtedly absorbed, and is eliminated by the kidneys, to whose secretion it imparts its odor. In *chronic pyelitis*, *chronic cystitis*, and *irritation of the bladder*, it is one of our best remedies, especially when, as is frequently the case, these diseases are associated with a generally-lowered systemic tone. As compared with turpentine, buchu is much less stimulating, and has a far more soothing effect upon the mucous membranes of the genito-urinary tract. In *irritated bladder*, when the urine is highly acid, and when there is a constant desire to urinate, with but little relief from micturition, buchu, in combination with a vegetable salt of potash and the sweet spirit of nitre, often gives great relief. The dose of the *fluid extract* (*Extractum Buchu Fluidum*, U. S.) is a teaspoonful, well diluted, given three or four times a day.

PAREIRA, U. S.—*Pareira Brava* is the root of Chondodendron tomentosum, a climbing plant of South America. There appear to be in the root one or more alkaloids (see *U. S. Dispensatory*, 15th ed., p. 1085). Pareira Brava has been used with asserted advantage in chronic *cystitis*, in "*irritable bladder*," and in chronic *gonorrhœa*, and appears to exert a stim-

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heart and motor nervous system. In the mammal small doses slow the pulse without affecting the vagi, whilst large doses paralyze the vagi and increase the pulse-rate. The blood-pressure is reduced by a direct action upon the vaso-motor centre. The secretion of urine is increased from five- to ninefold by even moderate doses.

ulant action upon the mucous membrane of the whole genito-urinary apparatus. It is said to be also tonic, and slightly aperient, so that it is especially valuable in urinary diseases when there is feebleness of digestion and a tendency to costiveness. The remedy should always be given in the form of the *infusion* (℥i–Oj), or *fluid extract* (*Extractum Pareiræ Fluidum*, U. S.), of which the doses are respectively a wineglassful and a teaspoonful three or four times a day.

Uva Ursi, U. S.—*Bearberry* is the leaves of the Arctostaphylos Uva Ursi, a low evergreen shrub, indigenous to northern maritime Europe, and also to our northern coasts as far south as New Jersey. They are from half an inch to an inch in length, wedge-shaped, thick, coriaceous, with a smooth, rounded margin. The odor is hay-like, the taste bitterish, astringent, and somewhat sweetish. Uva ursi contains gallic acid besides a crystalline principle discovered by Mr. J. C. C. Hughes (*Amer. Journ. Phar.*, 1847), and by him named *Ursin*, but now generally known as *Arbutin.* It occurs in long acicular colorless crystals, freely soluble in water, less so in alcohol and ether, and is resolved by the action of sulphuric acid into glucose and *hydrochinone.*

Therapeutics.—Uva ursi is capable of acting as a weak astringent, but has been long used in medicine for its influence upon the genito-urinary mucous membrane, and at present is employed only in chronic *pyelitis*, *cystitis*, and other affections of the genito-urinary mucous membrane, when a slightly stimulant and an astringent action is desired. Mr. Hughes found that in doses of one grain *arbutin* is a powerful diuretic. It seems to be free from poisonous properties, as Jablonowski (*Thesis*, Dorpat, 1858) took in forty-eight hours eighteen grammes of it without discomfort. It produces a discoloration of the urine varying from pale greenish to dark greenish brown, the color deepening upon standing. It has been proven by the researches of Von Mering (*Pflüger's Archiv*, Bd. 14, 1877, p. 276), of L. Lewin (*Virchow's Archiv.*, 1883, Bd. 92), and of Steffen (*Untersuchungen*, Wurzburg, 1883) that the discoloration of the urine is due to the breaking up of the arbutin in the body into glucose and hydrochinone. The change probably occurs in the kidneys, as arbutin is free from toxic properties, whilst Brieger has shown that hydrochinone is poisonous, producing in man giddiness, ringing in the ears, lessening in the force and frequency of the pulse, etc. The experiments of Lewin indicate that the arbutin is the active principle of uva ursi, and Forster (*Aerztl. Intelligenzblatt*, 1881) has shown that hydrochinone is a powerful disinfectant and anti-ferment. It is stated that a one per cent. solution will arrest putrefaction and alcoholic fermentations, whilst one-half per cent. is sufficient to check butyric fermentation. On the other hand, H. Paschkis (*Wien. Med. Presse*, Bd. 25, p. 13, 1884) states as the result of the practical use of arbutin in *gonorrhœa* and *cystitis*, that it does not effect much good, and that only a portion of it is changed into hydrochinone, most of it being eliminated as arbutin. He believes that uva ursi is of value in genito-urinary diseases, chiefly on account of its tannic acid and of the volatile oil which it contains. He affirms that the dried extract of the leaf, the best preparation, contains about three and one-half per cent. of arbutin to sixteen per cent. of tannic acid. In the hands, however, of Dr. Menche (*Centralblatt Klin. Med.*, 1883, p. 433), arbutin in doses of twelve grains a day has proven a very decided diuretic and very useful in *cystitis.* Whatever may be the value of arbutin, it is evident that the solid extract fully represents the drug, of which it is about four times the strength. It may be given in drachm doses three or four times a day. The dose of the *fluid extract* (*Extractum Uvæ Ursi Fluidum*, U. S.) is two to four fluidrachms three or four times a day.

CHIMAPHILA, U. S.—*Pipsissewa* is the dried leaves of the Chimaphila umbellata, a little indigenous perennial, distinguished from its inert congener C. maculata by the uniform glossy green of its leaves. The latter are about an inch and a half long, wedge-shaped, notched, pointed, and coriaceous. They contain tannic acid, bitter extractive, and, according to Mr. Samuel Fairbank, a crystalline principle, *Chimaphilin* (see *U. S. Dispensatory*). Pipsissewa is probably about equivalent to uva ursi in its therapeutic value, though perhaps not quite so actively *diuretic.* Prof. Geo. B. Wood (*Therapeutics*, vol. i. p. 133) commends it very highly in external *scrofula*, asserting that he has had a large experience with the remedy, and that in power over the disease it stands next to cod-liver oil and the preparations of iodine and iron. He believes that it acts not only as a mild astringent and tonic but also as an alterative, and states that its exhibition should be long continued, the administration being temporarily suspended whenever there is much fever. The remedy should be administered in the form of *decoction*, or of *fluid extract* (*Extractum Chimaphilæ Fluidum*, U. S.), the doses of which are respectively a wineglassful and a teaspoonful three or four times a day.

JUNIPERUS.—*Juniper* is the fruit of the common juniper of Europe and this country. These berries are round, bluish bodies, about the size of a large pea, of a sweetish, terebinthinate, aromatic taste. They owe their properties to a *volatile oil* (*Oleum Juniperi*), which is officinal. They yield to boiling water and to alcohol. Juniper is gently stimulant and cordial to the stomach. Upon the kidneys it exerts a decided stimulant action, and the oil freely given is capable of irritating the renal organs above the secreting-point, and of producing lessened secretion, strangury, and even suppression of urine. The volatile oil is undoubtedly absorbed, and chiefly escapes from the system through the kidneys. As a diuretic, juniper has two distinct uses. The most usual employment of it is as an adjuvant to cream of tartar or the alkaline diuretics. On account of its stimulant local influence upon the alimentary canal, it renders the cream of tartar far more acceptable to the stomach, and at the same time aids its diuretic action. Sometimes juniper is employed for its stimulant action on the mucous membrane of the genito urinary organs in *chronic pyelitis* and in *chronic catarrh of the bladder*. In the form of the *compound spirit* (*Spiritus Juniperi Compositus*, U. S.), or its equivalent, *gin*, juniper is often useful in the subacute *congestion* of the *kidneys* frequently seen in old persons, and characterized by aching in the loins without other more serious symptoms. The *infusion* is made by macerating an ounce of the berries in a pint of boiling water for an hour, the whole to be taken in divided doses during twenty-four hours. The dose of the oil is from five to fifteen drops; of the spirit, one tablespoonful.

Oleum Erigerontis, U. S.—*Erigeron Canadense*, or *Canada Fleabane*, contains a large proportion of a yellowish volatile oil of a rather pleasant odor and taste, which has properties resembling those of turpentine, but is much less stimulating. It may be employed in affections of the *genito-urinary organs*, and in passive *hemorrhages*. It is especially valuable in *menorrhagia*. According to Dr. Starke, it is very efficacious in *gonorrhœa* (*Lond. Med. Rec.*, 1876, p. 267). The dose is five to twenty drops every two or three hours, and is best administered on sugar.

The *stigmata of Zea Mays*, or Indian Corn, has been strongly recommended as a mild stimulant diuretic in both acute and chronic *inflammations* of the *bladder*, and in uric acid and phosphatic *gravel*, and, we are informed, is much used by several surgeons of this city. It is claimed that it has a distinct anæsthetic effect in allaying the pain of these affections, unless there be so much mucus as to prevent contact with the mucous membranes. M. Landrieux, of Paris, asserts that the urinary secretion is much increased, and the arterial tension distinctly augmented, even in cases of cardiac disease (*Med. and Surg. Reporter*, 1882, 103). Dr. Vauthier (*Arch. Méd. Belges*, Aug. 1880*) states that its activity depends upon *Maizenic acid.* It may be given *ad libitum* in infusion (two ounces to pint of boiling water); the dose of the fluid extract is one to two teaspoonfuls every two or three hours; of the maizenic acid, one-eighth of a grain. Dr. Ducasse gives half a drachm of the extract a day (*La France Méd.*, 1882, 811).

TEREBINTHINA—TURPENTINE.

Sufficient has already been said concerning the natural history of white turpentine (see page 126); but *Canada Turpentine* (Terebinthina Canadensis, U. S.), or *Canada Balsam*, as it is more commonly called, was not spoken of, because it is never used as a stimulant. It is the product of the Abies balsamea, or Balm of Gilead, or American Silver Fir, as it is variously named, a beautiful evergreen indigenous to the extreme northern United States and to the British Colonies. The juice is said to collect in little receptacles under the bark, and to be gathered by cutting these open and allowing them to drain into vessels. Canada Balsam is a thick and viscid but clear, yellowish liquid, containing, it is said, about twenty per cent. of volatile oil. The amount of the latter ingredient must vary greatly, since by age and exposure to the air the liquid balsam, losing its oil by evaporation and oxidation, becomes converted into a hard, brittle, translucent, resinous mass. Canada Balsam is very rarely, if ever, used in medicine.

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* Consult also *La France Méd.*, 1880, xxvii. 99; *La Union Méd.*, April, 1880; *Medical News*, vol. xliii. 372.

Oil of Turpentine, the volatile oil of ordinary turpentine, has already been considered; but it seems necessary to add here a few sentences in regard to its diuretic action and use. When moderate doses (ten drops every three hours) of turpentine are taken, there are usually no renal symptoms produced, except a slight increase of the urine. Somewhat larger amounts, when exhibited, are apt to give rise to aching in the loins and to frequent micturition, with perhaps urethral pain accompanying the act. If still larger quantities are ingested, these symptoms are intensified, and at the same time the secretion of urine is diminished. After very large repeated doses of the drug, the aching in the loins is very great, often with spasmodic pain in the ureters; a constant desire to pass water struggles with the inability to micturate, caused by the urethral spasm; the urine is very scanty, albuminous, and even bloody; priapism may be present, and an intolerable irritation may affect all the pelvic organs. These symptoms produced by overdoses of the drug show that its action upon the urino-genital organs is essentially and powerfully irritant, and that under all circumstances the existence of active irritation or inflammation of these organs absolutely contraindicates the use of oil of turpentine.

Oil of turpentine is never employed to increase the flow of urine for the purpose of affecting serous effusions. As a diuretic, it is used solely for its local influence upon the organs. *Excessive diuresis* sometimes is apparently dependent upon a relaxed condition of the kidneys, and under these circumstances oil of turpentine may be of great service. *Chronic pyelitis*, *chronic cystitis*, and *gleet* are all often very much benefited by the use of the drug.

In using the remedy in these cases, it should always be borne in mind that, with the exception of cantharides, it is the most actively stimulating of all the diuretics, and must be employed only when such a remedy is called for. In those comparatively rare cases of *urinary incontinence* which are dependent upon debility of the bladder, turpentine is sometimes of great service. When the same symptom is spasmodic, the remedy, of course, is harmful. In absolutely passive *hæmaturia*, in *impotence*, in certain conditions of *spermatorrhœa*, in *amenorrhœa* when great local debility exists, turpentine may be tried with fair hopes of its being useful. The dose of turpentine as a diuretic is ten to fifteen drops in emulsion, given from four to six times a day. If glycerine and oil of gaultheria be added to the emulsion in such proportion that half a teaspoonful of the one and one or two drops of the other be taken with each dose, they will almost completely disguise the taste of the remedy.

COPAIBA—COPAIBA. U.S.

The oleoresin of Copaifera multijuga and of other species of Copaifera, large trees growing in Brazil. Copaiba is a yellowish liquid of varying viscidity according to age, of a strong, terebinthinate, peculiar odor, and a bitter, burning, disagreeable taste. It mixes uniformly with absolute alcohol and volatile and fatty oils, and is readily dissolved by ether. It contains a volatile oil, a small quantity of a soft, viscid resin, and about fifty per cent. of a hard, acid resin. In 1829, Schweitzer (*Poggend. Annal.*, Bd. xvii. pp. 487 and 1095) announced that he had found in copaiba a peculiar crystallizable acid, *Copaivic Acid.* It is not in the plan of the present work to discuss elaborately the chemistry of drugs, and consequently I must remain content with the statement that the researches of Prof. Bernatzik (*Prager Viertel-jahrschrift*, Bd. c., 1868, p. 239) have shown that very frequently this crystalline acid does not exist in copaiba, and consequently that it is an unimportant constituent. Indeed, these researches seem to me to prove conclusively that copaiba is simply an oleoresin.

Physiological Action.—When given in therapeutic doses, copaiba has very little if any action upon the general system, and the influence even of very large amounts is often scarcely perceptible. In the researches of Bernatzik (*loc. cit.*, p. 251), eighteen grammes of the volatile oil were taken in three doses during twelve hours, and caused only an acceleration of a few beats per minute in the pulse-rate, and a rise of a fraction of a degree in the temperature, with, after a time, violent gastric and intestinal disturbance, evidently due to the local action of the drug, and characterized by vomiting and purging. Complete strangury was not produced, but there was some difficulty in passing the urine, which caused decided burning in the urethra. On the other hand, the action of the drug is much more decided upon some very susceptible persons, so that full doses of it produce decided fever, with increased frequency of pulse, and hot skin, accompanied almost always by decided symptoms of gastro-intestinal irritation. Sometimes, also, the urinary organs are more sensitive than usual to the action of the drug, so that strangury, and, as is stated by some authorities, even almost complete urinary suppression, may occur.

In 1841, Dr. G. O. Rey (quoted by Bernatzik) called attention to the fact that if nitric acid be added to the urine of persons taking copaiba, a precipitate is formed resembling that of albumen. This fact has been noted and commented on since its discovery by Dr. H. Weikart (*Archiv der Heilkunde*, 1860), by Dr. Rees (*Guy's Hosp. Rep.*, vol. xvii.), by Valentine (*Grundriss der Physiologie*), and by other observers. In order to produce the phenomenon with distinctness and certainty, it is seemingly necessary to use large doses of the drug, since Weikart failed to detect it after the exhibition of small amounts of copaiba oil. Various surmises as to the nature of this precipitate have been indulged in; but the experiments of Bernatzik *loc. cit.*, p. 252) appear to show that it consists of the oxidized oil united to some urinary principles. Dr. Bernatzik found that the elimination of the oil goes on slowly, continuing for as much as four days after its ingestion when large doses are employed. In his experiments with the resin of copaiba, the authority just noted exhibited fifteen grammes of it inside of five hours. It acted as an emeto-cathartic, causing a great deal of pain and irritation. The urine deposited very copiously on the addition of nitric acid, the resin seemingly being eliminated more abundantly than was the oil. Copaiba does not increase to any great extent the amount of the renal secretion, and no evidence has, that I am aware of, been offered to show that it affects materially the solids of the urine. Professor Quincke has recently found (*Archiv f. Experiment. Pathol. u. Pharmakol.*, xvii. p. 273, 1883) a new substance, *copaiba-red*, in the urine of persons taking the oil of copaiba. This substance is a colorless acid, forming easily soluble salts, and has the property of reducing the oxide of copper and polarizing to the left. It is colored red by sulphuric acid, gives a characteristic spectrum, and is soluble in water, chloroform, and amylic alcohol, but not in ether Its presence can be detected by warming the urine with concentrated sulphuric acid, when a rosy red color is produced, deepening into purple-red. The color may usually be developed by allowing the urine to stand with about five per cent. of sulphuric acid; a precipitate forms after a time, at first colorless, but finally becoming of a dirty violet. After the use of copaiba resin, the copaiba-red cannot be detected in the urine, but the urine still responds to Trommer's test for sugar. These facts are important as showing how a false diagnosis of diabetes might be made.

The clinical employment of copaiba has shown that the drug exerts its peculiar stimulant alterative action on other mucous membranes than those of the genito-urinary apparatus, and it is very possible that a slight elimination of the volatile oil takes place through the lungs.

THERAPEUTICS.—The chief use of copaiba in medicine is in *subacute* and *chronic inflammations* of the *genito-urinary* mucous membrane. In its action upon this structure it is a decided stimulant, but is less irritating and less stimulating than the oil of turpentine. *Gonorrhœa* is the disease in which it is mainly exhibited. It is especially useful in the advanced stages of this affection. If it be given in the beginning, before the inflammation has fully developed, it may sometimes succeed in aborting the attack, but, if it fail to accomplish this, may greatly aggravate the symptoms. During the height of the inflammatory stage, copaiba should not be employed. In other inflammatory affections of the genito-urinary mucous membrane, such as *pyelitis*, and chronic *cystitis*, when the disease is of a subacute or chronic character, the remedy may be employed, it being borne in mind that in its action it is much more stimulant than buchu or pareira brava, but much less so than turpentine.

In chronic *diarrhœa* and *dysentery*, copaiba is sometimes of use, through its local action on the diseased surfaces. The remedy has been highly recommended in the advanced stages of *bronchitis;* and in the chronic form of the disorder when attended by very free muco-purulent expectoration, I have occasionally employed it, with excellent results. Copaiba is sometimes used internally in *skin-affections*, but more frequently is employed externally as a stimulant dressing. The resinous mass which is left behind after the distillation of the oil of copaiba is stated to be an active hydragogue diuretic, increasing greatly the flow and lessening the specific gravity of the urine. In *dropsies* not dependent upon renal disease it is stated to be very efficacious given in doses of fifteen grains three times a day (*Guy's Hosp. Rep.*, 1876).

ADMINISTRATION.—The dose of copaiba is ten to twenty minims, repeated from three to six times a day, according to circumstances; the best effects are probably to be attained by the frequent use of small quantities. The medicine may be given dropped upon sugar, or, what is much better, exhibited in an aromatic emulsion, made with syrup and mucilage of gum-arabic in such a manner that a tablespoonful shall contain the required dose. When patients object to the taste, the drug may be given in gelatine capsules, each containing ten drops. It is said that these capsules do not, however, agree so well with delicate stomachs as the emulsion. When copaiba is rubbed up with magnesia, the resin unites with the earth to form a solid mass, in which the oil is mechanically held (*Massa Copaibæ*, U. S.). Pills made in this way are ineligible, being disintegrated and absorbed with difficulty. The *oil* (*Oleum Copaibæ*, U. S.), which is prepared by distillation, is isomeric with oil of turpentine. It may be exhibited in emulsion or in capsules, in doses of eight to fifteen minims.

CUBEBA—CUBEBS. U.S.

The unripe berries of the Piper Cubeba, a climbing plant of Java and other portions of the East Indies. These berries are blackish-veined, about the size of a small pea, and have attached to them a short stalk three or four lines long. Their odor is aromatic and peculiar; their taste warm, camphoraceous, and peculiar. Cubebs is a somewhat complex body, but there can be no doubt that the ethereal extract, or oleoresin, as it is commonly called, represents its medicinal virtues. The extract appears to consist chiefly of three substances: a volatile oil and the brown resinous substance formed by its oxidation, a peculiar acid, and a neutral crystallizable principle, *Cubebin*. *Cubebic Acid* was first discovered by Monheim, but has been especially examined by Prof. Bernatzik (*Prager Vierteljahrschrift*, 1864, Bd. lxxxi., p. 9). It is nearly tasteless, forms salts with the bases, has a very faintly acid reaction, and dissolves in concentrated sulphuric acid with the production of (according to Bernatzik) a purple-violet color, changing on the addition of a little water to a cherry-red, and altogether disappearing when further dilution is practiced.

PHYSIOLOGICAL ACTION.—In some respects, cubebs, when taken internally, resembles black pepper in its effects. It is, however, much less stimulating than its congener. After the ingestion of the ordinary therapeutic dose of cubebs, nothing unusual is experienced; but when very large amounts are taken there are evidences of gastric excitement, such as sensation of warmth in the stomach, slightly-increased frequency of pulse and heat of skin, with perhaps some giddiness or headache. The urine is slightly increased in amount, and acquires a peculiar odor. When very large doses are ingested, the symptoms of gastric irritation are more severe, and the subject suffers from gastric burning, nausea, vomiting, and colicky pains, with in some cases, purging.

An eruption resembling urticaria has been occasionally noticed after the exhibition of cubebs: it is exactly similar to the eruption sometimes caused by copaiba, and, like it, is probably due simply to gastric irritation.

That the active principles of cubebs are eliminated by the urine is well established, as, after the exhibition of the drug, when nitric acid is added to the urine, a precipitate, resembling somewhat that of albumen, occurs.

The most elaborate physiological study of cubebs that I have met with was made by Prof. Bernatzik (*loc. cit.*). This experimenter took himself, and gave to a student, ten grammes of the cubebate of magnesium. No decided symptoms were induced by this, further than some pulse-acceleration and gastric uneasiness; but the elimination of uric acid was greatly increased, and the cubebic acid was found in the urine. Half an ounce of the oil of cubebs was taken in thirty-six hours, the last three doses, aggregating ten grammes, being ingested in six hours. This was followed by very decided gastric irritation; by the appearance in the urine of the oil, not as it was ingested, but oxidized and in the form of a resin; the eliminated uric acid was about one-third in amount of that excreted after the exhibition of cubebic acid. Of the powdered cubebs, fifty grammes were taken in eight hours; the gastro-intestinal irritation was very marked; the nitric-acid precipitate was abundant in the urine; the elimination of uric acid was about midway between the extremes of the previous experiments. According to the researches of Prof. Bernatzik, *cubebin* is inert.

THERAPEUTICS.—Cubebs has been used to some extent for its local stimulant action upon the alimentary canal, but for this purpose is very inferior to black pepper and other spices. It is at present almost exclusively employed to influence the genito-urinary mucous membrane, in precisely those cases in which copaiba is exhibited. The two drugs have very nearly the same range of action, but the cubebs is less apt than is the copaiba to derange digestion. Very often the best effect in *gonorrhœa* and other genito-urinary disorders is obtained by giving the two remedies in combination. Cubebs is sometimes employed with asserted advantage in chronic *hæmorrhoids*, and also in those varieties of *bronchitis* in which copaiba is useful. It forms the basis of certain proprietary lozenges, much used by public speakers and others to relieve the relaxation of the larynx which follows slight colds or over-use. For this purpose the berries themselves may be chewed, and are very effectual. In *coryza*, the powdered drug used as a snuff has sometimes a beneficial effect. It should not be employed in the early stages before secretion has been established, but is indicated later in the affection, when the discharge is profuse.

ADMINISTRATION.—The dose of powdered cubebs is from half a drachm to three drachms, which may be exhibited in syrup or molasses three times a day. The volatile oil of cubebs (*Oleum Cubebæ*) is officinal, and may be given in emulsion three or four times a day, in the dose of fifteen drops, gradually increased to half a drachm, unless some effect is previously produced upon the urinary organs. This oil does not so thoroughly represent the crude drug as does the officinal *oleoresin* (*Oleoresina Cubebæ*), which may be given in doses of from ten to fifteen minims, increased as necessary. It is best administered in emulsion, but may be exhibited in the form of a bolus, enough sugar having been added to make a plastic mass. The *tincture* (*Tinctura Cubebæ*—1 to 10, U. S.) is an ineligible preparation; dose, f℥ii to f℥vi. The dose of the *fluid extract* (*Extractum Cubebæ Fluidum*, U. S.) is ten to forty minims.

MATICO, U. S.—*Matico*, the dried tops of the Piper angustifolium of Peru, contains a volatile oil, resin, and, it is said, a bitter principle, *Maticin*. It is largely employed as a styptic, and as such probably acts chiefly mechanically, coagulating the blood in its interstices, adhering to the wound, and thus arresting the hemorrhage. It has also been employed in internal *hemorrhages*, and in *gonorrhœa*. In these affections it probably acts similarly to oil of turpentine, although much less of a stimulant, and much more feeble. The *fluid extract* (*Extractum Matico Fluidum*, U. S.) and the *tincture* (*Tinctura Matico*—1 to 10, U. S.) may be respectively given in doses of forty-five minims and two fluidrachms.

CANTHARIS.—*Cantharides* is considered elsewhere in detail (see Epispastics), and it is only necessary here to say a few words in regard to its use in diseases of the genito-urinary tract. The active principle of Spanish flies is certainly eliminated by the kidneys, and acts therefore locally upon these organs, as well as upon those over which their secretion flows. The influence exerted by this means is simply one of intense irritation, cantharides being an irritant to these organs in any dose sufficiently large to have an effect. Indeed, of all the officinal drugs cantharides is the most actively irritant to the kidneys and subordinate organs. Consequently it is employed only when an intensely stimulant action is desired, as in obstinate *gleet*, in which affection it is often combined very advantageously with the tincture of chloride of iron. In *pyelitis* and *cystitis* it is very rarely indicated, but may be cautiously employed in very chronic cases. The *tincture* of cantharides is the only preparation used internally. For the dose and method of administration, see Epispastics.

CLASS IV.—DIAPHORETICS.

Diaphoretics are those medicines which are employed to increase the action of the skin. It is scarcely in place here to discuss the results of suppression of the functional activity of the skin or the importance of the surface-elimination to the system. It does seem well, however, to call attention to the fact that the perspiratory glands have a double function to perform,—that of elimination, already alluded to, and that of keeping down the temperature of the body during exposure to heat. When a man enters a Turkish bath the temperature of which is perhaps 160° F., or when he works in the sun on a very hot day, there is, if he be used to such exposure, little or no rise in the temperature of the body, because the surface-glands secrete sweat so actively as to expose a great amount for evaporation, and by the conversion of so much water into vapor such an amount of heat is absorbed—*i.e.*, converted from heat into repulsive force—that the body is cooler. The reason that even a moderate degree of heat in a moist atmosphere is intolerable is because evaporation cannot take place.

From what has already been stated, it is obvious that the use of dry external heat, or rather exposure to a hot atmosphere, is a powerful means of producing perspiration: it is, indeed, in healthy men the most powerful method at our command. It may be applied either in the form of the *Turkish bath*, in which the air of the hot chamber is very dry, or in the *Russian* or *vapor bath*, in which the atmosphere is surcharged with hot vapor. Very wonderful therapeutic properties have been ascribed to the direct action of heat (Urquhart, *Manual of the Turkish Bath*, London, 1865)* when applied by the Turkish bath; but the remedy appears to me to act only as a powerful sudorific, perhaps also doing good in some cases of acute internal congestion by attracting the blood to the surface and thereby depleting the interior. In private practice, or whenever a properly-provided bath cannot be commanded, a very efficient and readily-applied substitute consists of a large tin funnel furnished with a long bent beak, a stool with a hole in the centre of its seat, or else a few bricks, and a large spirit-lamp. The patient being closely wrapped up in bed, and the clothes being especially "tucked in" about the neck and shoulders, the funnel is placed upon the stool or the bricks in such a manner that the beak of it enters well under the bedclothes, coming close to but not in contact with the person of the sick man. The spirit-lamp, being then placed immediately under and close to the funnel, must, when lighted, send a column of hot air and vaporized water through the beak into the space around the body of the patient. When the lamp is sufficiently large, and a little care is taken to see that the nozzle of the funnel is not obstructed by the bedclothes, the process just detailed affords a very efficient method of giving a vapor-bath.

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* The term Turkish Bath is here applied to the bath used in this country under that name. This bath appears not to be a copy of the Oriental bath, but merely a derivative from it. According to a writer in the *British and Foreign Medico-Chirurgical Review* (vol. xxxvii. p. 87), in the East the sudarium, or sweating-chamber, rarely has a temperature of more than 98° F. Consult also *Bathing; How to Do It, When to Do It, and Where to Do It*, by E. Sheppard, London, 1865; *The Anglo-Turkish Bath*, by Y. J. Moore, London, 1865.

Hot-water baths offer another very successful method of inducing profuse perspiration. The patient should be placed in a bath of about 98° or 100° F., and remain there fifteen or twenty minutes, during which time, by the repeated addition of very hot water, the temperature should be raised to 110° F., or to such point as the patient can endure. Warmed blankets having been plentifully provided, the sick man should be lifted from the bath into them, be closely wrapped up, and so left for three or four hours before being transferred to the usual bed. According to Dr. A. Steffen (*Jahrb. für Kinderheilk.*, Hft. iii., 1871), after this use of the bath the body has been proven to undergo loss of weight continuously for one or two days.

Profuse sweating is always more or less exhausting, but is not nearly so much so as purging, and therefore may be practiced in dropsical patients too feeble to allow of the use of purgatives. The hot baths are not, however, altogether free from danger or objection. Sometimes in the Turkish and Russian baths the patient fails to sweat freely, and a feeling of distress, a bounding, rapid pulse, and perhaps severe headache, develop themselves: under these circumstances the bodily temperature rises, and a fever develops, which may go on to the production of a true "thermic fever," and perhaps terminate in sudden death. This is an exceedingly rare result, and one that never can occur if the patient is removed from the hot chamber so soon as any unpleasant symptoms are manifested. Sudden death has, I believe, taken place once from "sun-stroke" in a patient whilst taking the "Turkish bath," also once from "congestion of the lungs" (*Brit. Med. Jour.*, Oct. 1878).

The use of hot baths of any kind is, of course, contra-indicated by the existence of fever; but, according to Dr. Steffen, the hot-water baths are pre-eminently contra-indicated by the existence of congestion or œdema of the lungs, or of a tendency towards these disorders, since under such circumstances the bath greatly increases the disease, or precipitates a perhaps fatal attack. My own limited experience, so far as it has gone, has corroborated these statements of Steffen. I have seen, under the conditions mentioned, the most frightful dyspnœa result from the use of the hot-water bath, a dyspnœa which was apparently prevented from terminating fatally only by the removal of the patient from the bath-tub. If disturbance of the respiration come on during the bath, the patient should be immediately taken out, and, if the symptoms be urgent, cold water should be freely dashed over the head, neck, and chest.

Diaphoretics produce the desired result in various methods, which may be briefly considered under four headings, representing as many modes of action.

First. *By relaxing the skin.* As has already been sufficiently shown (see Cathartics, p. 420), there is a form of secretion, or perhaps it would be more correct to term it of leakage, from mucous membranes, which is distinctly paralytic in its mechanism. The same assertion may be made in regard to the skin: the colliquative so-called "night-sweats" of phthisis afford a familiar example of this, occurring as they do in profoundly debilitated subjects, and at such times as there is the greatest relaxation of the system,—*i.e.*, during sleep. The profuse sweats of collapse also may be instanced as examples of the general truth just enunciated. Normal processes which produce great relaxation cause great sweating: thus, during vomiting, especially if it be accompanied by much nausea, the skin pours out its secretion. By virtue of this general law certain remedies act as diaphoretics. All of the diaphoretics which cause sweating by producing relaxation, and which are employed in medicine, are nauseants, constituting a distinct group,—the *Nauseating Diaphoretics.*

Second. *By reducing the force of the circulation.* There is undoubtedly a condition of over-action or over-rapidity of the circulation in which the affected glands are unable to perform readily their normal functions. Thus, it is well known that the first stage of inflammation is one of arrested secretion, and that in high fever there is a general drying-up of the secretions. The skin does not differ from other organs in this respect: consequently its functional activity may fail because of excessive arterial action. Hence there is a class of remedies which, although perhaps not actively sudorific in health, are in disease very efficient in reducing the circulation and restoring the functional activity of the skin. It is evident that there is a close connection between the present mode of influence and that noted in the previous section; and it is no less apparent that the nauseant diaphoretics act most powerfully in reducing the circulation. There are, however, certain diaphoretics which act in the present method but are not nauseants: these sudorifics form a separate class by themselves,—the *Refrigerant Diaphoretics.*

Third. *By entering the circulation and directly stimulating the glands of the skin.* It appears to be a general law that when any medicinal principle is eliminated by any excretory organ, the general activity of that organ is increased by the effort at elimination. Thus, the vomiting and purging of arsenical or antimonial poisoning, the increased urinary secretion following the ingestion of a potassium salt, are apparently the results of attempted elimination. The skin undoubtedly eliminates medicinal substances, and is undoubtedly subject to the general law: consequently there is a class of remedies which increase its action by a direct influence.

It is manifest that a drug may relax the general system, may diminish the force of the circulation, and also may stimulate directly the skin: indeed, it is most probable that antimony does all of these; and at least some of the refrigerant diaphoretics probably act in the last two ways. There are, however, certain substances which seem to cause sweating purely by stimulating the function of the skin. These are in this work grouped as *Simple Diaphoretics.*

Fourth. *By filling up the blood-vessels.* There is much reason for believing that precisely as under certain circumstances water, by increasing the amount of the blood, will provoke increased renal secretion, so, under other circumstances, will it cause increased dermal excretion. The antagonism which exists between the skin and the kidneys in regard to the amount of their respective secretions has already been sufficiently dwelt upon (see p. 455). It seems well to reiterate, however, that warmth favors the action of the skin, whilst cold stimulates the renal activity. Thus, large draughts of water, if taken cold, the patient being kept cool, increase the urine, but, if they be taken hot, and the patient covered up warmly in bed, increase the perspiration.

Diaphoretics are employed in the practice of medicine to fulfil the following indications:

First. *To arrest forming diseases* of not very severe type, probably by causing a flow of blood to the surface, and thereby relieving slight internal congestions, and possibly by eliminating principles which have been retained in the blood instead of being excreted as they ought to have been. In *general cold*, in *muscular rheumatism*, *suppressed menstruation*, and other results of exposure to cold and of checked perspiration, the diaphoretics afford the most efficient means at our command for restoring the normal functions.

Second. *To favor absorption.* In *dropsy* the diaphoretics are of very great value, often aiding diuretics and purgatives in effecting a cure, and sometimes, when these fail, or when circumstances forbid their use, rescuing the patient from impending death. None of the medicinal diaphoretics except jaborandi are of sufficient power to be relied upon in dropsy. The Turkish, the Russian, and the hot-water bath are capable of producing sufficient sweating to cause absorption of dropsical fluid, but must be vigorously employed.

Third. *To aid in the subsidence of diseases* which naturally pass off with a sweat. The chief use of diaphoretics for this purpose is in *miasmatic fevers*, especially in the *remittent* form of the affection, when the sweating stage fails to develop itself thoroughly and the paroxysms run into one another. Even in the single paroxysm of *intermittent fever*, by hastening the closing stage, diaphoretics will often shorten the paroxysm.

Fourth. *To eliminate noxious materials* from the blood. The old humoral idea of the ground-work of such diseases as fevers, the belief in a distinct materies morbi which could be eliminated from the blood, has no sufficient demonstration to be accepted, and, although diaphoretics do good in *fevers*, yet it cannot be granted that it is in this manner. The very great power of increased diaphoresis in cooling the body through surface-evaporation has already been dwelt upon; and much of the good effected by diaphoretics in diseases of high temperature probably has its origin in this power. Modern science seems, however, clearly to point out that this class of remedies may aid in separating from the blood retained secretions, and may to some extent replace the action of the kidneys when these organs are disabled by disease.

In 1851, Dr. Schottin (*Archiv für Physiolog. Heilkunde*, Jahrg. xi.) discovered urea in the sweat of patients suffering from the collapse of cholera. Not only has the discovery of Schottin been confirmed by the researches of G. O. Rees (*Encyclopædia of Anatomy*, vol. iv. p. 841), of Fiedler (*Diss. Inaug.*, Leipsic, 1854), of Hirschsprung (*Gaz. des Hôpit.*, 1865), of Kaup and Jürgensen (*Deutsches Archiv für Klin. Med.*, Bd. vi., 1869, p. 54), of Leube (*Ibid.*, Bd. vii., 1869, p. 3), and of G. Deininger (*Ibid.*, p. 587), but it has also been abundantly proven that the skin excretes urea freely during the advanced stages of Bright's disease, and also during the partial urinary suppression of scarlatinal desquamative nephritis. The urea in renal disease may even form a distinct crystalline powder on the skin; but it is most abundant about the mouths of the sweat-glands. I believe Landerer was the first to announce that urea was present in the sweat of healthy persons; and, although chemists of excellence have been unable to detect it, yet its presence at times can no longer be denied, since it has been found not only by Landerer, but also by Funke in 1858 (*Moleschott's Untersuchungen*, Bd. vi.), by Meissner (*De Sudoris Secretione*, Diss. Inaug., Leipsic, 1859), and by Leube (*loc. cit.*); Fourcroy (quoted by Rees) has also found it in the sweat of horses. By a series of elaborate experiments, Leube (*loc. cit.*) has rendered it probable, if he has not actually proven, that in health there is such a relation between the skin and the kidneys that when the former is very active the latter excrete less than the normal amount of urea.

When to the facts already narrated are added the observation of Griesinger, that in diabetes the perspiration contains sugar, and the well-known circumstances that in rheumatism the sweat contains lactic acid, and in jaundice biliary products, the value of diaphoretics as a means of getting rid of retained excretions becomes manifest. For this reason, in Bright's disease, especially of the acute form, they are of the greatest value, acting beneficially in three different ways: by drawing the blood to the surface, and thereby relieving any internal congestions of the kidneys or other organs that may exist; by promoting the absorption of dropsical effusions; and by eliminating retained secretions.

NAUSEATING DIAPHORETICS.

The most frequently employed medicine of this class is *tartar emetic*. This substance is so fully discussed in the earlier portion of this book that very little need be said about it here. It seems well to point out, however, that the antimonials act as diuretics, even when not given in doses sufficient to cause nausea, and that they do so apparently in two ways,—by reducing the force of the arterial circulation, and by a direct action. They are probably eliminated to a very slight extent by the skin; although this has not, to my knowledge, been proven. Tartar emetic is to be employed as a diaphoretic in sthenic cases only, and is especially used in *inflammatory fevers*. The dose of it as a diaphoretic is from the sixth to the twelfth of a grain. If a diaphoresis is urgently demanded, the dose should be gradually increased until decided nausea is induced. An excellent combination in many cases is tartar emetic, neutral mixture, and a minute amount of morphia.

Ipecacuanha is another nauseating substance, which, like tartar emetic, seems to exert an influence upon the skin, even independently of its action on the stomach. Moreover, like the antimonials, it never in small doses by itself causes profuse sweating, but simply seems to aid in maintaining the insensible perspiration and in keeping the skin soft and pliable in inflammatory fevers. Partly for this reason it is frequently combined with mercury in such diseases as acute *peritonitis*. The diaphoretic dose of ipecacuanha is a grain every two hours. Some persons with delicate stomachs are decidedly nauseated by this amount; and to these only half a grain should be given at a time.

A very famous and efficient diaphoretic preparation of ipecacuanha is *Dover's Powder* (PULVIS IPECACUANHÆ ET OPII, U. S.), which contains one grain of opium, one grain of ipecacuanha, and eight grains of sugar of milk. Dover's powder is employed in two distinct methods. In some diseases, as in acute *rheumatism*, an opiate is indicated to allay pain or for some other purpose, and at the same time a diaphoretic is needed to keep up the action of the skin. Under these circumstances, from three to five grains of the compound powder of ipecacuanha may be given every two, three, or four hours, *pro re nata*. The medicine is more apt to nauseate when taken in powder than when exhibited in pills; for which reason the latter form of administration is preferable in the class of cases now under consideration, especially as the powder is to most persons a disagreeable medicine. In the second method of using Dover's powder, a single large dose is given for the purpose of producing profuse sweating. In the intense suffering which sometimes results from *suddenly suppressed menstruation*, the remedy is most efficient, alleviating the pain and aiding in the production of the desired diaphoresis. In breaking up a *cold*, or in *muscular rheumatism*, Dover's powder is often used to cause sweating (see Alcohol as a Diaphoretic).

REFRIGERANT DIAPHORETICS.

Aconite, *veratrum viride*, and all the various remedies used to depress the cardiac action when excited, are, in the strictest sense of the term, refrigerant diaphoretics. Sufficient has, however, already been said in regard to their use. The *citrate of potassium*, whether in the form of *effervescing draught* or of *neutral mixture*, is constantly employed in sthenic fevers, and affords, I think, the best basis there is for fever-mixtures in such cases, the more powerful depressants being added to it as circumstances demand.

SIMPLE DIAPHORETICS.

PILOCARPUS. U. S.—JABORANDI.

This drug, which has long been employed by the natives of South America, received its first notice, under the various names of *Jaborandi*, *Jaguarandy*, and *Jamguarandi*, from Dr. T. J. H. Langgard in his "Diccionario de Medecina domestica," Rio Janeiro, 1865. It attracted no attention, however, until 1874, when it was brought to Paris by M. Coutinho. Its botanical source is Pilocarpus pinnatus, a member of the rue family. The leaves are oval, elongated, entire, 1.2 to 1.5 inches long, and one-third to one-fourth as broad; their taste is bitter, and their odor hay-like, and depend upon the alkaloid, *pilocarpia*, discovered by Byarson.[*] The nitrate of pilocarpia is readily obtained in white lamellated crystals, and is soluble in eight parts of distilled water. The virtues appear to reside exclusively in the leaves and bark, Dr. Frerichs (*Berlin. Klin. Wochenschr.*, 1875) having found the wood inert.[†]

Physiological Action.—When an infusion of from sixty to ninety grains of jaborandi is given to an adult, in about ten minutes the face and neck become deeply flushed, and free perspiration and salivation commence. After a hypodermic injection of the alkaloid, the symptoms may set in in six minutes. The sweating begins on the face; both it and the salivation are excessively profuse, and last from three to five hours. There is not rarely nausea, and sometimes even vomiting. The pulse is usually more or less quickened, as is also frequently the respiration. After the sweating has ceased, the patient is left more or less exhausted. The nasal and lachrymal secretions are also very generally increased under the action of the drug, and M. Gubler has noted diarrhœa, which in the experiments of Ringer and others has not been present. There is sometimes contraction of the pupils and even disturbance of vision. These effects of the drug are in the adult fairly constant; but subjects have been occasionally found who were not susceptible to the action of the remedy, and, very curiously, in Dr. Ringer's experiments children were found to be very unsusceptible, although doses of sixty grains were employed. Schwann, M. Morat (*Lyon Méd.*, Juillet, 1882), and other observers have noticed in the lower animals that very violent gastric and intestinal movements are produced by the drug.

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[*] A second alkaloid has been discovered by E. Harnack and H. Meyer and named *jaborin* (*Arch. Exper. Path. und Pharm.*, xii). It is a derivative of pilocarpin, and is said frequently to contaminate the commercial alkaloid. Its discoverers assert that they have studied its action upon the heart, pupil, intestines, and salivary glands, and found it identical with that of atropia. Its presence has no doubt been the cause of some contradictory results obtained by experimenters.

[†] Under the name of Jaborandi various drugs other than the product of Pilocarpus pinnatus are sold in Brasil. As the Pilocarpus pinnatus has been found to be active when grown in France, it is probable that it might be successfully cultivated in our Southern States

Secretion.—The sweat produced by jaborandi is often enormous in quantity (nine to fifteen ounces by estimation). It is stated to be at first acid, then neutral, and finally clearly alkaline. Vulpian (*Leçons s. Subst. toxiq.*, Paris, 1881, 87) denies that even the first sweat has other than alkaline reaction, and believes, with MM. Luchsinger and Trumpy, that there has been a mistaken observation, due to the fact that the secretion of the sebiferous glands is acid. In the analyses of M. Robin the chlorides were found in excess, the carbonates and phosphates in very minute amount, and the urea in more than five times its normal proportion, the amount eliminated in the sweating being estimated at from ten to fifteen grains. MM. Hardy and Ball believed that in their experiments the average amount of urea eliminated by the skin was seventeen grains (*Journ. de Thérap.*, 1874). Pilicier noted in a dog with a gastric fistula great increase of the gastric juices (*Med. Centralb.*, 1876, 430); the biliary secretion appeared to be lessened. On the other hand, M. Morat (*Lyons Méd.*, July, 1882) has noted a temporary increase of the sugar in the blood, an evidence that the glycogenic function of the liver is stimulated. Dr. Hammerbacher has found the secretion of milk lessened (*Arch. Gesam. Physiolog.*, xxx. 236). Whether or not the urine is increased in healthy persons when pilocarpin is given in a single large dose may be considered uncertain, but the assertion of M. Gubler that the alkaloid administered in very small repeated doses has a marked diuretic influence has received clinical confirmation. Much interest attaches to the effect of jaborandi upon urea elimination, but it cannot be considered as determined, except that in various diseases the combined urinal and dermal elimination is greatly increased by the drug. Hardy and Ball state that in health urea elimination from the kidneys is diminished by the drug, whilst Prof. Tyson and Dr. Bruen have found it increased both in health and in disease. The experiments have, however, been too few, and especially the conditions of their performance too lax, for much importance to be attached to them.

There appears to be some relation between the flow of saliva and that of perspiration produced by jaborandi: if the one is very profuse the other is often, but not always, correspondingly scanty. Sometimes the salivation almost replaces the sweating (Féréol, *Journ. de Thérap.*, Jan. 1875); very frequently it commences before the sweating, and often it is more persistent. During it the mouth is warm, and there is often a feeling of tenseness about the maxillary glands. The saliva contains an abundance of salts and of ptyaline, as well as a small excess of urea (*Boston Med. and Surg. Journ.*, p. 347). Pilicier, it is true, states that the proportion of albuminous compounds, and especially of sulphocyanide of potassium, is much diminished, but in M. Robin's analyses the proportion was even beyond the normal, and Ch. Bougarel has by careful experimentation shown that the power of jaborandi-saliva in converting starch into sugar is equal to that of the normal secretion. According to I. N. Langley (*Brit. Med. Journ.*, p. 247), in the frog the mouth and skin, after the exhibition of jaborandi, become covered with a viscid secretion; in the dog and the rabbit and cat there is profuse salivation. The effect upon the salivary secretion must be due to a direct influence upon the gland, as it is produced equally well after section of all of the salivary nerves (Langley, *Journ. of Physiology*, 1878, 339; Carville, *Journ. de Thérap.*, 1875; confirmed by Schwann, *Med. Centralb.*, 1875, p. 440); also when the drug is injected directly into the gland and prevented from entering the general circulation (Langley). According to the elaborate experiments of Langley, very small doses cause in the cat great increase of the secretion. Stimulation either of the chorda or of the sympathetic nerve causes respectively some increase or lessening of the secretion, but this increase or lessening is not nearly equal to that which occurs in the normal animal, and is due to the action of the nerves upon the circulation, and not to any influence of their secretory fibres. Very large doses of the drug injected into the gland immediately arrest the secretion, and doses of less size given in the same way, whilst increasing secretion, paralyze both chorda tympani and sympathetic nerves, so that stimulation of them has no effect. It is probable from the last fact that jaborandi has an action upon the secretory gland-cells.

Although the evidence just deduced indicates that an influence is exerted by jaborandi upon the gland-cells, the fact that atropia arrests the jaborandi salivary secretion prevents us from considering it settled that the drug does so act upon the salivary gland-cells rather than upon the peripheral nerve-endings, since there is reason for believing that the sweating which the drug causes is due to an action on the nerve-endings. Dr. Fuchsinger (confirmed by Nawrocki) has found that section of the nerves of the cat's leg did not prevent the paws from sweating when jaborandi was exhibited. This demonstrates that the action of the drug is peripheral, not centric. Five or six days after the section, when the peripheral nerve-endings had undergone degeneration, Fuchsinger found that jaborandi was unable to excite sweating. This, however, can hardly be considered to absolutely prove, as Fuchsinger claims, that the drug acts upon the peripheral nerve-endings, and not directly upon the glandular cells themselves, since it is probable that these glandular cells shared the anatomical changes of the nerve-endings (*Pflüger's Archiv*, xv. 482).

Jaborandi appears to stimulate the nutrition of the hair, and Prof. Prentiss, of Washington, has reported several cases in which the continued internal use of pilocarpin caused the hair to become exceedingly coarse and to change its color from light to dark (*Philad. Med. Times*, xi. 610). Dr. H. Rasori has noticed a tuberculated eruption apparently produced by jaborandi (*Trans. Intern. Med. Congress*, 1881, iii. 146). M. Grocco has found that pilocarpin, hypodermically injected or locally applied, sensibly affects hysterical anæsthesia (*Lond. Med. Record*, 1882, 137).

Temperature.—The action on the bodily heat varies somewhat. M. Robin affirms that before and during the early stages of the sweating from jaborandi the temperature rises 1° to 2° F., but afterwards falls as much below the normal point, and remains depressed for one or two days. This primary rise of temperature has been noted by other observers (Ringer, *Lancet*, i., 1873, 157; Greene, *Phila. Med. Times*, vi. 56; Scotti, *Berlin. Klin. Woch.*, 1877, 141; Pilicier,* *Med. Centralb.*, 1876, 429; Weber, *Ibid.*, 770), but is certainly frequently absent altogether or very trifling.† The subsequent fall of temperature seems to be a very constant phenomenon when the action of the drug is sufficiently severe; it probably depends in great part, or altogether, upon the loss of heat during the sweating.

Circulation.—The action of jaborandi upon the circulation has been studied by Mr. Langley (*Journ. of Anatomy*, x. 188), E. Leyden (*Berlin. Klin. Wochenschr.*, 1877, 406), Kahler and Sayka (*Med. Centralb.*, 1876, 541), and Harnack and Meyer (*loc. cit.*, p. 374). The phenomena noted by these observers are in most respects in accord, but Kahler and Sayka using the extract of jaborandi, and E. Leyden commercial pilocarpin, have found the pulse either as a constant or occasional phenomena at first increased in its rate, whilst Harnack has never seen this with chemically pure pilocarpin. Immediately after the injection of the alkaloid into the jugular vein the arterial pressure falls, but in a few moments the characteristic phenomena of a slow pulse with increased arterial pressure come on. This slowing of the pulse is not prevented by previous section of the pneumogastric, but is at once set aside by an injection of atropia (Langley, Leyden, Harnack, and Meyer): as is also the diastolic arrest of heart which pilocarpin produces in the frog. Harnack and Meyer therefore believe that both in the frog and the mammal the chief cardiac influence of the alkaloid is exerted upon the intracardiac inhibitory ganglia: but Prof. Ringer (*Practitioner*, xxvi.

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* Pilicier noted that the rise occurred in the axilla, but not in the rectum; this would indicate that it is a local phenomenon, the result of a heating of the *surface*, not of the interior, of the body.

† Consult Riegel, *Berlin. Klin. Wochens.*, 1875, 86; Bardenhewer, *Ibid.*, 1877, 8; Auschmann, *Ibid.*, 353.

12) finds that jaborandi and atropia act antagonistically upon the ventricles separated from the auricles, and as the ventricles contain no inhibitory ganglia, some other explanation of the antagonism must be found.* The rise of the arterial pressure is stated by Harnack and Meyer to be prevented by the use of curari and artificial respiration, and to be, therefore, a secondary, not direct, result of the drug's action; it is probably due to the convulsive muscular contractions produced by the drug. In the latter stage of the poisoning the arterial pressure falls. As in the experiments of Harnack and Meyer asphyxia in this stage did not cause rise of pressure, although the heart appeared still to retain its force, the vaso-motor system is probably paralyzed. The pulse still continues slow, although, according to Harnack, the vagi are completely paralyzed.

Sexual Organs.—Jaborandi does not appear to have any power over the sexual organs, except the pregnant womb. Cases of abortion during its use have been reported by M. Masmann (quoted by Larvand, *La Pilocarpine*, 1883) and by Schanta (*Wiener Med. Wochens.*, No. 18, 1878), but in the hands of other observers the drug has appeared to have little, if any, abortifacient influence, and M. Hyernaux and M. Chanteril have found it powerless in the lower animals (quoted by Larvand). When, however, the pregnant female is at her full term, the drug may affect the uterine contractions, as Larvand and others have noted an increase of the pains, or even a precipitation of labor, both in women and lower animals. Nevertheless, the oxytocic powers of jaborandi are very feeble. (See *British Medical Journal*, 1879, ii. 509; also, *Wien. Med. Blatt.*, 1879, vol. ii., 1178, 1207.)

Motor System.—In man, muscular tremblings have been observed during the action of jaborandi, but it is doubtful whether they are due to a direct action of the remedy. In the frog, as first noticed by Murrell (*Pharm. Journ. and Trans.*, vi. 228), small doses (3 mgrm. of pilocarpin) produce violent convulsions with heightened reflex activity, whilst larger amounts cause complete palsy. According to Harnack and Meyer the convulsions are due to spinal stimulation, and the paralysis partly to overwhelming of the spinal centres, and partly to paralysis of the muscles, the motor nerves themselves not being affected. In man and the higher animals convulsive movements have been noted, but the action of the drug upon the musculo-nervous system is entirely subservient to its other effects.

Eye.—When applied to the eye pilocarpin produces great contraction of the pupil, tension of the accommodative apparatus, and an approximation of the nearest and farthest points of distinct vision (Jno. Tweedy, *Lancet*, 1875, i.

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* Prof. Ringer's explanation seems at present the most probable. It is—that pilocarpin paralyzes the heart by combining with the molecules of the excito-motor apparatus and of the muscular tissue, and that atropia displaces the pilocarpin and thereby substitutes its own action.

159; C. Scotti, *Berl. Klin. Woch.*, 1877, 143; Galezowski (*Med. Times and Gaz.*, 1877, ii. 358). Mr. Tweedy also states that there is impairment of vision, due to benumbing of the retina. According to P. Albertoni the myosis is followed by a moderate but persistent mydriasis, and is not prevented by previous section of the oculo-motor nerve or of the upper cervical sympathetic ganglion. It is certainly the result of a peripheral influence. Galezowski, who uses a solution of one part of a pilocarpin salt in fifty parts of water, affirms that it answers as well as a solution of eserina in diseases of the eye, and has the great advantage of not producing irritation.

THERAPEUTICS.—Jaborandi is so powerful and certain in its diaphoretic action that it has already taken rank as the most reliable and influential of the remedies of its class; indeed, so great is its power that it has widely extended the use of diaphoretics. It is doubtful how far it is applicable to the treatment of fevers, although the decided lowering of the temperature by it would indicate a power over such bodily conditions. In *bilious* and other *malarial fevers* it is probably of value, but sufficient use has not as yet been made of it to determine its exact powers in hastening the desired remission. In *typhoid* and other *asthenic fevers* it would probably do much injury. In *dropsies* it has been widely employed, and certainly is a most efficient remedy. It appears to be as safe in asthenic *dropsies* as in any other remedy comparable with it in power, although in my own observation a free jaborandi sweat is almost as exhausting as a purging. Great value has been ascribed to it in facilitating the removal of *local watery effusions*, such as occur in *pleurisy*, etc. Cases of *pulmonic œdema* have been reported in which lives seem to have been saved by its employment. In *uræmia* it is the most efficient remedy at our command. In *acute* or *chronic Bright's disease* it is of great value, sufficing often in the one case to bring about convalescence, and in the other greatly to prolong life and make it comfortable. The sweats may be repeated daily, bi-weekly, or weekly, according to the circumstances of the case. There is one point in connection with this use of the drug which needs further study,—*i.e.*, the action of the remedy on the kidney itself. Purjesz (*Deutsch. Arch. Klin. Med.*, xvii., p. 533) has noted one case in which the drug seemed to produce albuminuria, but the occurrence may have been accidental, and there is some clinical experience in favor of the plan of giving the pilocarpin in doses of one-tenth of a grain three times a day, so as to avoid any violent action upon the skin and get a decided increase of the urine. Still, the case of Purjesz, and the occasional occurrence of strangury after the drug (my own experience, also Stumpf, *Deutsch. Archiv*, xvi.) would indicate that it stimulates the urinary organs, and that some caution must be exercised in its employment in the earliest stages of *acute tubular nephritis*. In *subacute and muscular rheumatism* it is very efficient. Prof. Ringer has reported several cases of *unilateral sweating* cured by the use of full doses of pilocarpin given hypodermically (*London Pract.*, xvii., p. 401), and it has been used with asserted success in *alopecia*. It has been extensively used in *diphtheria* and *croup*, but has no direct influence over the disease, and may do great harm in adynamic conditions: by increasing the glandular secretion of the bronchial tubes it may aid in loosening the membranes.

Locally applied (half-ounce of the leaves) in the form of a poultice, jaborandi may sometimes produce local sweating only, but I have seen very marked and extraordinarily prolonged general sweating so caused.

ADMINISTRATION.—The dose of jaborandi is forty grains to a fluidrachm. The *fluid extract* (*Extractum Pilocarpi Fluidum*, U. S.) may be used in doses of half a drachm to a drachm. Pilocarpin is superior to jaborandi in the certainty of its action, and in being less disagreeable, and probably less apt to nauseate. Weber, Bardenhewer, and Auschmann agree that 0.3 of a grain of it is equal to seventy-five grains of the best leaves; but this is probably an over-estimate of its powers. In the form of the *hydrochlorate* (*Pilocarpinæ Hydrochloras*, U. S.) it may be used hypodermically in watery solution, the dose being from one-eighth to one-third of a grain. Dr. Demme, of Berne, gives to children between one and two years old 0.075 grain; between two and six, 0.1 to 0.15 grain; between six and twelve, 0.15 to 0.35 grain, and finds it to work very well (*Med. Times and Gaz.*, 1877, ii. 636). No fatal results have as yet been reported, although Auschmann has twice seen alarming collapse follow moderate doses, apparently produced by excessive vomiting (*Berl. Klin. Wochenschr.*, 1877, p. 356).*

Antagonism with Atropia.—In February, 1875 (*British Med. Journal*), Mr. Langley called attention to the antagonism existing between jaborandi and belladonna. When the heart has been slowed or arrested by jaborandi, atropia will bring the rate of pulsation almost to normal; the reverse of this also occurs, provided the amount of atropia previously applied has not been too great (Langley, *Journ. Anat.*, x. 194). Upon the sweat-glands the two drugs have also antagonistic powers, one being able to annul the action of the other (Luchsinger, *loc. cit.*). The same is true in regard to the salivary secretion (Langley). This antagonism between atropia and jaborandi is affirmed by H. Larvand to extend to the intestines and pupil. In belladonna-poisoning the alkaloid has been used, with no advantage, in very small dose (*Lancet*, i. 1876, 346), but in a case in which nine-tenths of a grain of atropia had been taken, nine grains of pilocarpin are said to have been injected hypodermically in between one and two hours with success (Prof. Purjesz, *Pest. Med.-Chir. Presse*, 1880). Dr. L. Juhász reports (*Klin. Monatsbl. f. Augenheilk.*, xx. 86) a case in which it was estimated that about one and a half grains of atropia were taken, followed in half an hour by vomiting; four and a half grains of pilocarpin were injected in about seven hours, with a favorable result. Dr. Hofferts reports (*Wien. Med.*

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* A case of poisoning to which I have not had access, in *Bull. and Mem. Soc. de Thérap.*, sér. 2, v. 88.

Presse, 1883, xxiv. 1412) a case in which 7.5 grains of extract of belladonna were ingested, and nearly two grains of pilocarpin given, with recovery.

LIQUOR AMMONII ACETATIS—SOLUTION OF THE ACETATE OF AMMONIUM. U.S.

Spirit of Mindererus is prepared by saturating dilute acetic acid with the carbonate of ammonium, and consequently consists of a solution of the acetate of ammonium, containing as much of free carbonic acid as the water will absorb. It is a colorless liquid, and should have no odor, or a very faint odor of acetic acid. Any specimen having an ammoniacal odor should be rejected, as containing an objectionable excess of the carbonate of ammonium. The taste is disagreeable and saline. As the solution upon standing undergoes decomposition after a time, it should be freshly prepared when needed.

THERAPEUTICS.—Spirit of Mindererus appears to be a feeble stimulant diaphoretic. Cullen has known eight ounces of it to be taken in a very short time without inducing any effect; yet the testimony is very strong as to its having some value in disease, and in *adynamic fevers* it may be employed as a diaphoretic. It is, however, much less efficient than the sweet spirit of nitre, and is probably to most persons more disagreeable than that favorite drug. Special value has been claimed for it in *dysmenorrhœa*, and even in *menorrhagia;* but I do not believe that it has any superiority over other diaphoretics in the former affection, and its being of any use in the latter disease seems apocryphal. The dose is one to two tablespoonfuls.

SPIRITUS ÆTHERIS NITROSI—SPIRIT OF NITROUS ETHER. U.S.

Sweet spirit of nitre is prepared by adding sulphuric acid to alcohol, then adding copper wire, and after this nitric acid, distilling at a temperature not exceeding 180° F., and adding alcohol to the distillate. The first reaction which takes place between the sulphuric acid and the alcohol results in the liberation of ether, the hydrated oxide of ethyl; the nitric acid, giving to the copper two of its equivalents of oxygen, is converted into nitrous acid, which combines with the oxide of ethyl to form a nitrite. Spirit of nitrous ether is a volatile, inflammable liquid, of a pale-yellow color inclining slightly to green, having a fragrant, ethereal odor, free from pungency, and a sharp, burning taste. It slightly reddens litmus, but does not cause effervescence when a crystal of bicarbonate of potassium is dropped into it. When mixed with half its volume of officinal solution of potassa previously diluted with an equal measure of distilled water, it assumes a yellow color, which slightly deepens, without becoming brown, in twelve hours. A portion of the spirit in a test-tube half filled with it, plunged into water heated to 145° and held there until it has acquired that temperature, will boil distinctly on the addition of a few small pieces of glass. Spirit of nitrous ether has the specific gravity 0.837, and contains five per cent. of its peculiar ether. It should not be long kept, as it becomes strongly acid by age.

Physiological Action.—Undoubtedly, the sweet spirit of nitre, if taken in sufficient amount, acts very decidedly upon the organism. Mr. D. R. Brown reports (*Pharm. Jour. Trans.*, March, 1857) the effects of the inhalation of sweet spirit of nitre. The first symptoms are a bluish-purple, livid discoloration of the lips and fingers, and a peculiar pallor of the face. These increase, the face assumes a ghastly look, the extremities grow cold, and the pulse becomes very weak and frequent, but the breathing remains slow and regular; muscular weakness is extreme, and the least exertion causes hurried respiration, with painful oppression in the chest, and cardiac distress. Confusion of mind and giddiness may or may not occur, but headache always comes on sooner or later. In sufficient amount sweet spirit of nitre is undoubtedly an active poison. Dr. Christison reports the case of a woman whose death was attributed to it, and between three and four ounces killed a child three years old in twelve hours, the symptoms closely resembling those of alcoholic poisoning with the addition of vomiting and purging (*London Lancet*, 1878, ii.). In therapeutic doses it has no marked action, except in increasing the secretion of the skin and kidneys, and in a slight degree stimulating the nervous system. In children it is often of value as an antispasmodic.

Therapeutics.—Sweet spirit of nitre is one of the most popular of the diaphoretics. As it exerts a stimulant action, it is useful in *adynamic* rather than in sthenic *fevers*. In children with fever offering nervous symptoms, such as starting, jerkings, etc., it is especially useful. If the patient be kept about and cool, instead of being warmly covered in bed, spirit of nitrous ether acts as a decided diuretic; but it is not sufficiently powerful to make it worthy of reliance in *dropsy*. The dose of sweet spirit of nitre is: for an adult, a teaspoonful to a tablespoonful; for a child three years old, half a teaspoonful. If a diaphoretic action is required, very minute doses should be exhibited at short intervals. Thus, for a child a year old, a teaspoonful should be put in five ounces of water, and a tablespoonful given every hour.

Alcohol.—As is known to every hard drinker, alcohol when taken in excess, and especially if drunk with hot water, is eliminated by the skin, and often causes profuse sweating. As a diaphoretic it is, however, used in medicine for only one purpose,—*i.e.*, in those cases, such as a forming "*cold*," *subacute rheumatism*, and *suppressed menstruation*, when a single profuse sweating is desired. In these cases I have found the following plan most efficacious, provided the patient have not decided fever: a Dover's powder is administered, and directly after this the patient goes into a hot-water or vapor bath, or else does what is known in common parlance as "soaking his feet,"—*i.e.*, takes a pediluvium. The proper method of doing the former of these acts has been sufficiently described. In taking a foot-bath the patient should use a tub of sufficient size to enable him to place in it his feet and legs up to the knees; the water should be as hot as can be borne, and, as the feet become a little accustomed to the temperature, hotter water should be added; the immersion should continue fifteen or twenty minutes; during it, the patient, being in his night-clothes, should be well wrapped up in blankets, and at the close should be so transferred to the bed as not to get in any way chilled. After he has got to bed, and has been heavily covered with blankets, the patient should drink one or two tumblerfuls of a very hot and strong lemonade, containing one, two, or three tablespoonfuls of whisky or brandy.

I think the popular belief that after a sweat there is a greater liability than usual to take cold is well founded: care must, therefore, be exercised to avoid any exposure for a day or two. Anointing the skin with oil of sweet almonds, or with other equally bland fat, appears to have some effect in preventing the deleterious effects of cold after sweating.

WARBURG'S TINCTURE.—This is a dark-brown liquid, prepared in accordance with a very complicated formula,* which has obtained an extraordinary reputation in India and other tropical countries in the treatment of severe *remittent* and malignant *malarial fevers*. The testimony is so strong as to its remarkable and almost certain efficiency that it cannot be questioned, and entitles the tincture to rank above all other remedies. The method of administration is as follows: the bowels having been freely opened, a half-ounce of the tincture is given undiluted, all drink being withheld, and at the end of three hours a second half-ounce is in similar manner exhibited. Soon after the last dose a profuse and very aromatic perspiration sets in, and convalescence is usually secured. The remedy is also highly commended in acute *nervous exhaustion* and sudden *collapse* without organic disease.

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* For formula, see *Med. Times and Gaz.*, 1875, ii. 541; or *Phila. Med. Times*, vi. 136; or *London Practitioner*, xviii. 82.

CLASS V.—EXPECTORANTS.

THESE are medicines possessed of the power of modifying the secretions and thereby influencing the inflammatory conditions of the respiratory mucous membranes. There are various, and even opposing, methods, in accordance with which drugs act upon the pulmonary surfaces. In certain states of the latter, as in the first stages of acute bronchitis, the irritation of the part is too great for secretion, the first stage of inflammation being, as is well known, connected with suspension of function: in this condition the so-called *sedative expectorants* are indicated. These are remedies which lower arterial action: they are all nauseants, and the increase of bronchial secretion by them is analogous to that which they produce in the skin. In order to get their full effect, they must be given in nauseating doses; and if these are gradually increased until emesis is induced, the fullest therapeutic influence will be obtained. There are other drugs which may be termed *stimulating expectorants*, and which act directly upon the bronchial mucous membrane, some of them perhaps increasing secretion, but most of them rather modifying it, and some of them even diminishing it, by toning up a relaxed, over-secreting mucous membrane. Some substances which can hardly be called expectorants are nevertheless useful in bronchial diseases: thus, gallic acid will sometimes lessen the large quantities of mucus secreted in *bronchorrhœa;* or, when the mucus is tenacious in *chronic bronchitis*, alkalies will frequently be of great service by rendering it less viscid and thereby facilitating expectoration.

In many cases of disease occurring in the very young and in the very old, mucus may so accumulate in the lungs, owing to the inability of the enfeebled powers to force it up, as seriously to embarrass, or even fatally compromit, respiration. Very frequently, in acute cases of this character, such as the *suffocative catarrh* of infants, mechanical emetics are of the greatest service; but in chronic cases they induce so much disturbance of digestion as to render their use dangerous, and alcohol, carbonate of ammonium, oil of garlic or of turpentine, and other drugs capable of increasing the bronchial muscular power or activity, have to be relied upon.

Again, in certain conditions of the lungs, especially in *chronic catarrhal pneumonia*, iodine and other alteratives are of great value in facilitating the absorption of exuded materials; yet these remedies can hardly be called expectorants. It may be affirmed that the value of true expectorants in *pneumonia* of any variety is exceedingly problematic, and, except it be the muriate of ammonia, they far more often do harm in the chronic varieties by deranging digestion than they do good by influencing the lung-tissue.

There are several substances, chief among them being morphia, hyoscyamus, and hydrocyanic acid, which have the power of allaying cough and lessening irritation by an anodyne action. In regard to morphia, its property of checking secretion should not be forgotten, but should not prevent its use. These narcotics are especially useful when the cough is disproportionate to the amount of inflammation. When large quantities of mucus are being secreted in debilitated subjects, their use requires great caution, for fear of benumbing the nerves or nerve-centres and thereby increasing the danger of an accumulation of phlegm in the lungs.

Expectorants may be arranged under two heads: the nauseant or sedative expectorants, and the stimulating expectorants; and the general proposition may be laid down that expectorants of the first class are to be used in the first stages of acute bronchitis, whilst expectorants of the second class are to be employed in the advanced stages or in the chronic varieties of the disease. As these diseased conditions gradually merge into one another, so must the practitioner balance the ingredients of his expectorant mixtures, adapting their relations to the individual case.

The present seems a fitting place to say what is necessary in regard to the use of drugs by *atomization.* In this method of administration, a solution of the medicine employed is broken up by a mechanical contrivance into a fine spray and projected into the back of the mouth. There can be no doubt that when the operation is properly performed the spray reaches even the finest ramifications of the pulmonary bronchi. A discussion of this is at present scarcely necessary. Any reader having doubt upon the subject will find the evidence in the work of Dr. J. Solis Cohen (*Inhalation: its Therapeutics and Practice*, Phila., 1867).

The following rules should be attended to, to secure successful results:

1. Use the steam atomizers: all other forms of apparatus give irregular or too feeble currents, and should be discarded.

2. See that the points of the atomizing tubes are sharp and clean,—not foul, cracked, or with their edges worn.

3. See that the steam is generated equably and with sufficient force, and that the solution used is free from all solid particles, and, unless otherwise ordered, about the temperature of the body.

4. Never allow inhalations when the patient is excited, directly after eating, or immediately after exercise, unless especial circumstances, as in hæmoptysis, demand haste.

5. Have the glass mouth-speculum inserted well into the mouth, and the line of its axis and of the propulsion of the spray coincident with that of the mouth

6. When the pharynx, or even the larynx only, is to be reached, the operation is very simple, and respiration should be natural; but when it is desired to make applications to the ultimate bronchi, the respirations should be regular, slow, and as deep and full as possible, the lungs being well emptied at expiration.

7. Do not protract the sitting until the patient is fatigued. Five minutes is generally long enough to commence with. In hæmoptysis, this rule may sometimes be departed from with advantage.

8. Let the patient give his whole attention to the matter in hand.

9. In chronic disease, one, two, or three inhalations a day are usually sufficient. In acute disease, they may be required much more often, as every hour in diphtheria.

10. Never use atomization for the purpose of general medication: it is simply a method of applying substances locally to the respiratory organs.

The substances used by atomization may be conveniently arranged as follows:*

DILUENTS.—The only diluent of any value is *warm water*. In acutely *inflamed conditions* of the *mucous membrane*, the very frequent application of water at about the temperature of 90° F. will often afford marked relief, especially in *laryngitis*.

ASTRINGENTS.—These are employed to arrest excessive secretion or hemorrhage. In their use, it must always be remembered that they are more or less irritant, and that whilst some persons bear them very well, in others they produce very harmful irritation; also, that the idiosyncrasies of patients vary, so that whilst one person will best bear a certain one of the astringents, a second may be less irritated by another drug. The rule is to try carefully until the pulmonary idiosyncrasies are known. In cases of excessive *bronchial secretion*, any irritation sufficiently severe to give origin to tightness in the chest, or to much coughing, calls for the withdrawal of the medicine. In *hæmoptysis*, a greater risk can be judiciously assumed. The astringent substances employed in this way are: First, *tannic acid*, one to twenty grains to the fluidounce of water. I have not used this; but it is said to be well adapted to cases of free secretion. Second, *alum*, varying in strength from a solution of five grains to the ounce to a saturated solution. This I have used with great satisfaction. In *hæmoptysis*, only the strongest preparation is of avail; in *bronchorrhœa*, a weak solution should be employed at first, and the strength increased *pro re nata*. One advantage this drug has over tannic acid is its compatibility with the sulphate of morphia, which should always be added to its solution when any tendency to irritation exists. In *chronic bronchitis* with excessive expectoration, I have seen alum produce most gratifying results. Third, preparations of *iron:* of these the solution of the perchloride has been used in Great Britain and on the Continent; but Monsel's solution (Liquor Ferri Subsulphatis) is much preferable, as even more powerfully styptic and less irritating. Ten drops of the solution may be added to the fluidounce of water and be used for the trial dose. If the lungs will bear it and necessity exists for a stronger solution, the strength may be carefully increased up to half a fluidrachm to the ounce. *Acetate of lead* is at once astringent and sedative. It has been recommended by Beigel and by Fieber in the advanced stages of acute catarrhs, in the proportion of three to ten grains to the fluidounce.

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* Recently attention has been called to the inhalation of fresh, almost nascent vapors of muriate of ammonia. By means of a very simple apparatus, air loaded with muriatic acid vapor is drawn at each inspiration through a weak water of ammonia, and of course reaches the lung saturated with the vapors of the muriate. Dr. Leberman (*Brit. For. Med.-Chir. Rev.*, 1874, i. 518) affirms that he has employed this with the happiest results in one hundred and two cases of *granular sore throat, chronic bronchitis, asthma, whooping-cough*, and even *angina pectoris!* Most druggists, I believe, keep the inhalers.

NARCOTICS.—When there is great laryngeal or even bronchial irritation, especially in the *laryngitis* of advanced *phthisis*, half a grain of morphia, or a drachm of tincture of hyoscyamus, will often afford very great relief. It must not be forgotten that the constitutional effect of the narcotic may be produced in this way.

SOLVENTS.—As is well known, in certain respiratory affections it is very important to get rid of a false membrane, or exudation, which appears upon the mucous surfaces. Some substances seem to exert at least a degree of solvent power upon this material. Of these, lime-water appears to be the most effective and the least irritant. It should be used pure. (See article on Lime (*post*); also consult Meigs and Pepper, *Diseases of Children*, Phila., 1874, p. 680.)

ALTERATIVES.—In chronic *bronchitis*, and even in chronic *catarrhal pneumonia*, or *phthisis*, balsamic vapors have long been used, but atomization is not necessary in their application. *Muriate of ammonia* may, however, be so applied: in chronic bronchial *catarrh* it is sometimes advantageous, and in acute *laryngitis* inhalations of a warm saturated solution of it are often very useful. In chronic *laryngitis*, nitrate of silver may be exhibited by atomization, but it is, I think, much better to apply it directly by means of the laryngoscope and the brush or probang. In cases of *fetid expectoration*, carbolic acid in weak solution (gtt. i–ii to f℥i) may be used as an antiseptic and alterant.

NAUSEATING EXPECTORANTS.

The three nauseating expectorants are ipecacuanha, tartar emetic, and lobelia. As these substances are sufficiently discussed elsewhere in this work, it remains only to say a few words in regard to their comparative use as expectorants.

Lobelia is used only when the inflammatory action is complicated with a tendency to spasm of the bronchial muscles. It is too powerfully depressant to be given to children with safety. The best expectorant preparation is the *tincture* (*Tinctura Lobeliæ*, U. S.). The ordinary expectorant dose of this is twenty to thirty drops, usually given in combination every three hours. When a very decided impression is desired, as in some cases of asthma, one fluidrachm may be exhibited every two hours, until vomiting is produced or relief obtained. Under these circumstances, the patient should be closely watched, as lobelia in these large doses sometimes causes very alarming symptoms.

Ipecacuanha is the safest and most used, although perhaps the least powerful, of all the nauseating expectorants. It is the only one that should be given freely to children. In the early stages of all acute inflammatory conditions of the respiratory mucous membranes it is of great service. The preparation most generally used in acute *bronchitis* is the syrup, the dose of which is from twenty drops to a teaspoonful, every two, three, or four hours, according to the exigencies of the case. Any of the other liquid preparations of ipecacuanha may be employed in a corresponding dose. The *Ipecacuanha Lozenges* (*Trochisci Ipecacuanhæ*, U. S.) each contain about one-quarter of a grain of ipecac, and may be employed in catarrhal complaints. The troches of ipecacuanha and of morphine (*Trochisci Morphinæ et Ipecacuanhæ*, U. S.) contain each the fortieth of a grain of sulphate of morphine and the twelfth of a grain of ipecacuanha, and may be used when an anodyne effect is desirable.

Tartar Emetic is much more powerful than ipecacuanha as a sedative and nauseant, and must be used with more care. It is the most efficient of all the sedative expectorants, and affords in cases of urgency a very efficacious, although a very disagreeable, method of putting an end to an attack of acute *bronchitis*. I have known of a public speaker, who had risen in the morning completely overwhelmed with bronchitis, enabled to deliver his evening speech by the judicious use of tartar emetic. To effect this rapid relief, one-twelfth of a grain of tartar emetic should be taken every ten or fifteen minutes until it induces profuse vomiting. After the nausea is passed, the system may be toned up for exertion by a lunch of ale and oysters. Tartar emetic is a powerful remedy, and is especially injurious to young children, in whom it is very apt to induce collapse. It is therefore contra-indicated by infancy, as it also is by the existence of gastro-intestinal inflammation. The dose as an expectorant is from one-twelfth to one-quarter of a grain, repeated according to circumstances.

STIMULATING EXPECTORANTS.

AMMONII CHLORIDUM—CHLORIDE OF AMMONIUM. U.S.

$(NH_3HCl - NH_4Cl.)$

Muriate of Ammonia, or *Sal Ammoniac*, is prepared by heating with chloride of sodium the sulphate of ammonium, which is obtained from gas-liquor by the addition of sulphuric acid. *Gas-liquor* is a water which has been used to wash ordinary burning-gas, and contains largely of the carbonate, hydrocyanate, hydrosulphate, and sulphate of ammonium. The *sulphate of ammonium* is not itself employed as a medicine, but is officinal, because the other preparations of ammonia are made from it.

The muriate of ammonia is a white, translucent, fibrous, and tough salt, free from odor, but having a sharp, saline taste. It occurs in large concavo-convex plates, dissolves in three parts of cold and in one of boiling water, and at a red heat sublimes without decomposition.

Physiological Action.—When applied in a solid form, or in a concentrated solution, the chloride of ammonium acts as an irritant upon raw surfaces and upon mucous membranes. This influence seems, however, not to be sufficiently powerful to enable the drug in any dose to produce lethal poisoning: at least, Oesterlen (*Heilmittellehre*, Tübingen, 1851) states that one of his patients took two ounces of the salt without suffering any more severe results than colicky pains and some diarrhœa.

If some of the older experimenters are to be credited, its influence upon the lower animals is more powerful. In the experiments of Dr. Smith (quoted by Stillé), two drachms of the salt applied to the wounded thigh of a dog caused death in from twelve to thirty-six hours, and, according to Orfila, the same quantity dissolved in two ounces of water and introduced into the stomach of a dog caused violent convulsions, with great tetanic rigidity, and finally death. Arnold (Wibmer, *Die Wirkungen der Arzneien und Gifte*, Munich, 1831, Bd. i. p. 143) found that thirty grains will kill a rabbit in ten minutes. On the other hand, in the recent studies of Dr. Rabuteau (*L'Union Médicale*, 1871, p. 330), half a drachm injected into the veins of a moderate-sized dog had no apparent effect, whilst one drachm only produced muscular weakness, deepening into temporary paralysis of the hind legs, vomiting without diarrhœa, and general prostration for four or five hours.

The chief interest of the clinician in the physiological action of the muriate of ammonia centres in its effects when given continuously for some time. The older writers upon the subject assert that its influence on the heart is a sedative one, but that it increases the capillary circulation (Sundelin, *Heilmittellehre*, Band i. p. 150, Berlin, 1853). This opinion appears to me to be founded chiefly upon speculation and inference, and not to have any sufficient basis. Whatever may be the action of very large amounts, I have never been able to perceive that the muriate of ammonia, given in ordinary doses, has any decided influence upon the circulation. According to Sundelin and other authorities, the drug, when given freely and continuously, produces a profound impression upon the blood itself, lessening its plasticity and impairing its constitution. One case of profound and otherwise inexplicable prostration and typhoid condition, which occurred in a patient who was taking nearly a half-ounce of muriate of ammonia per diem, has come under my own notice; and Dr. Isham reports (*Med. News*, xl. 455) a case in which an eruption of bloody blebs, with hæmaturia, hemorrhages from mucous membranes, and great prostration, was apparently produced by the prolonged use of the salt. The elaborate analyses of F. W. Böcker (*Beiträge zur Heilkunde*, Bd. ii. p. 170, Crefeld, 1849), although somewhat discordant, indicate that sal ammoniac does impoverish the blood, since in some instances there was a decided decrease in its solids. Arnold (*loc. cit.*) also noticed that in dogs poisoned with the muriate of ammonia the blood contained less than the normal percentage of solids. In accord with this reputed action on the blood is the effect of the drug upon the urinary secretion. In a very elaborate series of experiments, Böcker (*loc. cit.*, p. 158) found that, given to a healthy man, sal ammoniac increased very notably all the solids of the urine, except the uric acid, which was very slightly diminished; and Rabuteau, in an investigation in which, by identity of diet, etc., all sources of fallacy were as far as possible excluded, found that the excretion of urea was very decidedly increased.

The opinion has long prevailed that the muriate of ammonia especially affects the mucous membranes, and Böcker believes that in them it hastens very greatly the nutritive changes and the exfoliation of epithelium. Clinical experience has, I think, demonstrated that the drug does act especially upon the mucous membranes; although it is very difficult to bring forward any definite tangible proof of this.

The muriate of ammonia, when ingested, probably enters into all the excretions, since Rabuteau (*L'Union Médicale*, t. xii. p. 329, 1871) has found it in the saliva. The same observer has shown that the chief elimination takes place through the kidneys, since he found in the urine almost all of the salt that had been taken.

THERAPEUTICS.—In the last century the chloride of ammonium was very extensively used in *intermittent fever;* but at present the salt is rarely or never employed, although Aran (*Bulletin Thérapeutique*, t. xii. p. 344) has attempted to revive the practice, and asserts that he has had very good effects resulting from it,—in thirteen cases of intermittent fever curing, by the exhibition of two drachms a day, seven at once, four after the second paroxysm, one after the third, and one after the fourth. The chief present use of the muriate of ammonia is as a remedy in *acute* and in *chronic bronchitis:* in the first variety of the disease the drug should not be exhibited in the first stages; but after active inflammatory action has been subdued by the sedative expectorants, it is very useful. It is very largely employed in the *catarrhs* of young children, and is often of great service. In Germany the remedy has been extensively exhibited in *gastric* and *intestinal catarrhs;* Dr. W. Stewart,* as the result of a large experience, highly commends its use in *chronic torpor* of the *liver*, *chronic hepatitis*, and *hepatic abscess*. In the first of these affections I have employed it to a limited extent, with very good effects. Dr. Stewart gives twenty grains of it three times a day, and continues its use for weeks or even months.

In various *neuralgias*, especially in the *ovarian* variety, but to a less extent in *migraine* and other forms, sal ammoniac has been largely employed for the purpose of relieving pain. Thirty grains of it are given in combination with from two to five drops of tincture of aconite root, and the dose is repeated in half an hour, if necessary.

ADMINISTRATION.—The usual dose of the muriate of ammonia in catarrh is from five to ten grains three or four times a day. This dose is given in a tablespoonful of water, to which, for the purpose of concealing the taste, from five to ten grains of liquorice may be added. The *troches* (*Trochisci Ammonii Chloridi*, U. S.) contain two grains each, and are used as a local stimulant to the fauces and the epiglottis.

SENEGA—SENEKA. U. S.

The root of Polygala Senega, a small, herbaceous perennial, indigenous to the Middle and Southern United States. This root is several inches long, very much contorted, of a peculiar feeble odor, and a taste at first sweetish but afterwards acrid. It is distinguished by a keel-like line, shorter than the root, and presenting the appearance as if a string were drawn tightly under the bark from end to end. Quevenne discovered in seneka a peculiar principle which he named *Polygalic Acid*, although he thought that it was closely allied to saponin. According to Husemann (*Die Pflanzenstoffe*, p. 751), the more recent researches of Bolley (*Ann. Chem. Pharm.*, xc., xci.) have shown that it is identical with *saponin*, a glucoside first found in the root of Saponaria officinalis, but now known to exist in a great many plants. It is a white, amorphous powder, of a neutral reaction, odorless, but very irritating to the nostrils, and having an acrid, burning taste. It is very soluble in water, to which, even when in no greater quantity than one part in a thousand, it imparts the property of foaming like soap-suds, when shaken.

THERAPEUTICS.—Seneka is chiefly used as a stimulant to the mucous membrane of the lungs in *chronic bronchitis* and in the very advanced stages of the acute disorder. It is believed to be one of the most stimulant substances of its class, and is therefore contra-indicated by acute pulmonary inflammation and is indicated by a relaxed state of the bronchial mucous membranes. If its stimulant effect be modified by combination with tartar emetic, it may be given in acute bronchitis at an earlier stage than it could be used by itself. Seneka is locally irritant, and, when administered in large doses, produces vomiting, which is probably reflex in its origin. In overdoses it not only vomits, but also purges: it is, however, never used for these purposes. Seneka has been employed as an emmenagogue in *amenorrhœa* and as a diuretic in *dropsy*, but has achieved no permanent reputation in these disorders. The *abstract* (*Abstractum Senegæ*, U. S., dose, five to ten grains) and the *fluid extract* (*Extractum Senegæ Fluidum*, U. S., dose, ten to fifteen drops) are officinal, but the *syrup* (*Syrupus Senegæ*, U. S., dose, a fluidrachm) is usually employed.

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* Chloride of Ammonium, Rangoon, 1870; *Madras Monthly Journ. Med. Sci.*, Febr., March, 1872; *Indian Med. Gaz.*, Dec. 1872; *Phila. Med. Times*, viii. 316.

AMMONIACUM—AMMONIAC. U. S.

The concrete juice of an umbelliferous plant, Dorema Ammoniacum, a native of Persia. It is said to exude from punctures made in the plants, and also to be obtained by a process similar to that employed in the case of assafœtida. It is a gum resin, containing a little volatile oil, and occurs in commerce as irregularly globular yellowish tears, from the size of a pin to that of a large chestnut, hard and brittle when cold, and breaking with a smooth, resinous fracture; and in irregular mottled masses, composed in part of tears, and containing many impurities. The odor is faint and disagreeable, the taste bitterish, sweetish, and somewhat acrid.

THERAPEUTICS.—The influence of ammoniac upon the general system is very slight. It is a local irritant, and therefore in large doses is capable of producing vomiting and purging. It was formerly employed as a nervous stimulant, but its internal use is now restricted almost exclusively to *chronic bronchitis* with either deficient or excessive secretion. The dose of it is twenty to thirty grains; of the officinal *mixture* (*Mistura Ammoniaci*, U. S.), a tablespoonful. There are two officinal plasters of ammoniac: the *Emplastrum Ammoniaci*, which is used as a mild counter-irritant and as a local stimulant to promote the resolution of *scrofulous tumors* or *enlarged joints;* and the *Emplastrum Ammoniaci cum Hydrargyro*, which contains mercury and sulphur, and is employed as a local stimulant, alterative, and discutient in the same affections as the first-named plaster, and in *syphilitic nodes* and *tumors;* its external use is said to have caused salivation.

BENZOINUM—BENZOIN. U. S.

The concrete juice of Styrax Benzoin, a large tree, native of Peru. The drug is said to be obtained by incising the tree and allowing the juice to harden as it exudes. The finest specimens of benzoin consist of tears agglutinated together; the poorest, of brown or blackish masses without tears. The fracture is resinous, the surface of the tears smooth and whitish, the odor fragrant, the taste at first very slight, afterwards somewhat acrid. The chief constituents of benzoin are resin and benzoic acid; cinnamic acid is also frequently present, and is said to be especially found in the white tears.

Benzoic Acid (ACIDUM BENZOICUM, U. S.) is obtained by sublimation of gum benzoin. As thus prepared, it is in white feathery crystals, of a silky lustre and a fragrant vanilla-like odor, due to the presence of a volatile oil, the pure acid being inodorous. The taste is warm, acrid, peculiar. Benzoic acid melts at 250°, and volatilizes without change; is soluble in two hundred parts of cold and in twenty-four parts of boiling water; is soluble in alcohol, fixed oil, and alkaline solutions. It is a feeble acid, but forms neutral salts with the alkalies. Benzoic acid is widely distributed through the vegetable kingdom, constituting the peculiar principle of all true balsams, and is occasionally present in the urine of grass-eating animals. It is a normal constituent of castor, and has been detected by Seligsohn (*Chemische Centralblatt*, 1861) in the suprarenal capsules of an ox. It is used considerably in the arts, and for this purpose is prepared from the allied hippuric acid of horse-urine, and also, it is said, from naphthalen.

PHYSIOLOGICAL ACTION.—Locally applied, benzoic acid is a decided irritant, and its vapors, when inhaled, produce bronchial catarrh.

Our knowledge of the action of benzoic acid upon man and the higher animals is very limited. In ordinary therapeutic doses it exerts no perceptible influence upon man, except it may in the production of gastric irritation, with consequent nausea and vomiting. Thus, Schreiber took in two days about half an ounce of the acid, and suffered only a feeling of abdominal warmth, spreading over the whole body, and accompanied by an increase of the pulse-rate amounting to thirty beats per minute, by increased secretion and excretion of phlegm, with slight disturbance of digestion.

Very few experiments with benzoic acid upon the lower mammals have been reported. W. Grube (*Centralb. f. Chirurg.*, 1876, p. 777) states that in massive doses (1 to 5766 of animal's weight) it produces intoxication, with disturbance of circulation and respiration, and paralysis of the hind feet, and that the antipyretic influence of benzoic acid is greater than that of salicylic acid.

Especial interest attaches to the elimination of benzoic acid, because, as was first discovered in dogs by Wöhler, and afterwards in man by Ure, it appears in the urine, united with nitrogenous atoms, as hippuric acid.* It becomes a matter of great interest to know where this change occurs; but this has only recently been certainly determined. Kuhne and Hallwachs thought that the conversion occurred in the liver; but the more recent researches of Meissner and Shepard (*Untersuchungen über das Entstehen der Hippursäure in thierischen Organismus*, Hanover, 1866) appear to show that it really takes place in the kidneys. Certainly it does not happen in the intestines or in the blood, since after the exhibition of large doses of benzoic acid it alone can be detected in the blood; and after the administration to rabbits by the mouth of large amounts of hippuric acid, only traces of the latter, with large quantities of benzoic acid, can be found in the blood, although the hippuric acid reappears in the urine;* further, moderate amounts of hippuric acid injected into the blood cause severe symptoms of poisoning, which is not true of benzoic acid. When very large amounts of benzoic acid are introduced into the blood, a portion escapes through the kidneys unchanged.† These experiments are confirmed by G. Bunge and C. Schmiedeberg, who also found that in the dog with renal arteries tied no conversion of benzoic acid into hippuric occurred, but that tying of the ureters did not interfere with the change. They have also succeeded in converting benzoic into hippuric acid by passing blood containing benzoic acid, with or without glycocoll, slowly through the kidneys, removed from the body directly after death. From some of their experiments it would seem that the blood-corpuscles play an important rôle in the process, as when serum freed from blood-corpuscles was used, at most only a trace of hippuric was formed. According to Meissner and Shepard, sometimes the benzoic acid is converted into succinic acid instead of hippuric acid in man, and in chickens it is habitually changed into two new products, one of which is nitrogenous. The point as to whence the nitrogen necessary for the formation of the hippuric acid is obtained has not yet been clearly made out. In the elaborate experiments of Carl Virchow (*Zeitsch. f. Physiol. Chem.*, vi.) there was a decided increase produced by benzoate of sodium of the nitrogenous elimination from the kidneys; but the testimony as to the effect of the ingestion of benzoic acid upon the urea and uric acid of the urine is singularly contradictory. Thus, Ure (*Medico-Chirurg. Trans.*, xxiv. 30, 1841), Leroy d'Etiolles (quoted by Stillé), and Debouy (quoted by Stillé) all affirm that the uric acid is very much diminished or altogether absent, whilst Garrod (*Memoirs of the Chem. Soc.*, i., 1842, and *London Lancet*, Nov. 1844) and Keller (*Ann. der Chem. und Pharm.*, xliii., 1842) assert that its quantity remains normal. Again, Garrod affirms that the urea is very much diminished in quantity, whilst Keller and Meissner and Shepard (*loc. cit.*) declare that it is not affected. The only logical conclusion would seem to be that the effect of benzoic acid upon the urine is variable. All authorities appear to agree, however, in asserting that the acidity is increased.

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* Gusseron found hippuric acid in urine of a new-born child when benzoic acid had been given to the mother just before the birth (*Hoffmann und Schwalbe's Jahresb.*, 1879, 283).

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* This alleged conversion of hippuric acid is not thoroughly established, and has given rise to much discussion. For a general summary and latest information, see paper by Van de Velde and Stockvis, *Arch. Exper. Patholog. u. Pharm.*, xvii. 189.

† According to the experiments of Th. Weyl and B. von Anrep, if benzoic acid be given to man or animals in a febrile state a much larger proportion of it than usual is eliminated unchanged (*Hoffmann und Schwalbe's Jahresb.*, 1881, 447).

In April, 1872, Dougall (*Med. Times and Gaz.*, i. 1872) announced that benzoic acid is one of the most active of antiseptic drugs. Since this publication, numerous experiments have been made by E. Salkowski (*Berlin. Klin. Wochens.*, 1875, 297), Grube (*Centralb. f. Chirurg.*, 1876, 778), by Bucholtz (*Archiv Experim. Pathol. und Pharm.*, Bd. iv.), Fleck (Benzoësäure, etc., *München*, 1875), with the unanimous result of ascribing to benzoic acid a first rank in destroying bacteria and preventing putrefaction. In most of these investigations benzoic acid was found to be much more active than salicylic acid. Bucholtz found that 0.02 per cent. of benzoic acid had a very perceptible effect upon the development of bacteria, and 0.1 per cent. inhibited entirely their growth; also that the benzoate of sodium was no less active than the pure acid.

THERAPEUTICS.—Benzoic acid, or gum benzoin, was formerly very freely exhibited in *chronic bronchial catarrh* as a stimulant expectorant; at present it is not much employed. The chief use of it is in urinary affections. Dr. Ure first suggested and commended its employment in uric acid *gravel* and *calculus*, because, as he thought, it diminishes the excretion of uric acid: as its possession of this power has been strenuously denied, the theory of its use in uric acid gravel is exceedingly doubtful. No less an authority, however, than Dr. Golding Bird* asserts that clinical experience has shown its value in *uric acid diathesis*. In the *phosphatic urine* of *vesical catarrh*, benzoic acid may be employed with much advantage. By rendering the urine more acid it increases its power of dissolving the phosphates, and at the same time it exerts a stimulant action upon the mucous membrane of the bladder. Dr. Lamaire affirms that benzoic acid (fifteen grains in twenty-four hours) given along with cannabis indica acts most happily in acute *gonorrhœa* (*Phil. Med. Times*, iv. 638).

Since the discovery of the antizymotic power of benzoic acid, it has been used to some extent in Germany as a remedy in *diphtheria*, *erysipelas*, and allied diseases with asserted good results. Two or three drachms of the benzoate of soda are given during the twenty-four hours. Prof. Senator, of Berlin, states that, given in sufficient dose, benzoic acid is as much of a specific in *acute rheumatism* as is salicylic acid. He gives it in daily doses of from two to three drachms, and states that larger amounts may be employed with impunity; the benzoate of sodium is preferred to the pure acid as of easier solubility (*Allegem. Wien. Med. Zeitung*, 1878, xxiii.).

Benzoic acid has the property of preventing animal fats from becoming rancid, and is therefore much used as an addition to ointments. Moreover, it exerts a peculiar, often very beneficial, stimulant action upon the skin, and is very useful in such conditions as *chapped* hands, lips,* or nipples, and even in *fissure* of the *anus.*

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* *Urinary Deposits*, Philadelphia, 1859, p. 160. Dr. Bird states that he has found the following formula of great service in chronic uric acid gravel:. ℞ Sodii carbonatis, ʒiss; acidi benzoici, gr. xl; sodii phosphatis, ʒiii; aquæ ferventis, f℥iv; solve et adde aquæ cinnamomi, f℥viiss; tincturæ hyoscyami, fʒiv. S.—Two tablespoonfuls three times a day.

There would seem to be no doubt but that benzoic acid may be substituted for carbolic or salicylic acid in antiseptic surgery. Under the name of *balsamum traumaticum* a preparation practically the same as the compound tincture of balsam was formerly much used as a vulnerary. The practice has gone out of vogue; but the discoveries concerning antisepsis and the excellent results obtained by Mr. Bryant (*Lancet,* ii., 1876, 747) show that it was well founded. Mr. Bryant simply covers the wound in compound fractures and other severe injuries with lint thoroughly saturated with the compound tincture of benzoin, and maintains absolute quiet with non-removal of the dressing for some days. His results appear to challenge those obtained by the most complicated antiseptic surgery (see also *Lancet,* 1877, i. 671).

ADMINISTRATION.—The dose of benzoic acid is from ten to thirty grains. Gum benzoin is never used itself, but in the form of the *tincture* (*Tinctura Benzoini*—1 to 5, U. S.),—dose, fℨss to fℨi; of the *compound tincture* (*Tinctura Benzoini Composita,* U. S.), used in chronic bronchial catarrh,—dose, fℨi to fℨii. *Adeps Benzoinatus,* U. S., contains only enough of the benzoin to preserve the lard, and is employed as the basis of ointments.

BALSAMUM PERUVIANUM, or *Balsam of Peru,* is obtained from the Myrospermum Peruiferum, a tree of Central America, by making incisions in such places as have been previously beaten with clubs, slightly burning them, catching the juice in old rags, and finally boiling these in water and skimming off the balsam as it rises to the surface. This balsam is a viscid, honey-like, fragrant, brownish fluid, of a warm, bitterish taste. According to Frémy, it contains not benzoic, but cinnamic acid. It has been used in chronic *catarrhs* of the respiratory and the genito-urinary system, in doses of half a fluidrachm.

BALSAMUM TOLUTANUM, or *Balsam of Tolu,* is obtained from a tree very closely allied to that which yields the balsam of Peru, if indeed it be not identical with it. The incisions, however, are not burnt, and the juice is simply caught in vessels. Balsam of Tolu is at first a thick, viscid fluid, but by time it is converted into a hard, translucent, resinous solid. Its odor is highly fragrant, and its taste vanilla-like. It contains *cinnamic acid* and a volatile oil, and its medical properties are the same as those of the balsam of Peru. On account, however, of its grateful taste, it is preferred to the latter, and is very much used to flavor medicines, especially cough-mixtures. In large doses (gr. xx to xxx every three hours) it may be of some value in chronic catarrh, but as generally used its preparations are simply agreeable vehicles. The dose of the *tincture* (*Tinctura Tolutana*—1 to 10, U. S.) is one-half to one fluidrachm; of the much more frequently used *syrup* (*Syrupus Tolutanus,* U. S.), half a fluidounce.

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* Prof. Stillé commends a mixture of one part of the compound tincture of benzoin and four parts of glycerine.

ALLIUM, U. S., or *English Garlic*, the clove of the Allium sativum, contains a volatile oil, which is a stimulant in small doses to digestion, and is also a stimulating expectorant often of very great service in certain stages of *bronchitis*. It is in lingering, deep-seated "*colds*" that I have derived especial benefit from its use. It is also very valuable in the *acute bronchitis* of infants, when the powers of the system begin to give out. The oil of garlic is further believed to have the ability to stimulate the expulsive function of the small bronchial tubes, and is certainly a powerful rubefacient and a decided nervous stimulant. For these reasons, garlic poultices are a favorite application in the acute *suffocative catarrh* of infants, and are not rarely applied to the spine, legs, and feet in general *infantile convulsions*. They are made by simply reducing the garlic to a pulp by pounding. When a continuous application is desirable to the delicate skin of an infant, as in catarrh, it is generally necessary to reduce their strength with flaxseed meal.

SCILLA, or *Squill*, is one of the most used and most efficient of the stimulating expectorants, coming especially into play in the advanced stages of ordinary *bronchitis*. The *syrup* (*Syrupus Scillæ*, U. S.) is the favorite expectorant preparation. As it contains acetic acid, it is incompatible with the carbonate of ammonium. The *Compound Syrup of Squill* (*Syrupus Scillæ Compositus*, U. S.: squill, seneka, āā one hundred and twenty parts; tartar emetic, three parts to two thousand parts) contains one grain of tartar emetic to the ounce, and is therefore sedative to the circulation, although stimulant to the bronchial mucous membrane. It is, of course, in large doses a powerful emetic; and, under the name of *Coxe's Hive Syrup*, it is very frequently used in the domestic treatment of croup. The dose of the simple syrup is one-half to one fluidrachm; of the compound, twenty to forty drops; as an emetic to children, ten drops to a fluidrachm, according to age, repeated every twenty minutes until it operates.

PIX LIQUIDA.—*Tar* is a black semi-liquid substance, of peculiar odor and taste, obtained by the destructive distillation of various species of pine. The tar used in this country is almost exclusively the product of the Pinus palustris of North Carolina and other of the Southern States. In composition it is very complex, containing pyroligneous acid, creasote, empyreumatic oil, and a number of more or less peculiar principles. When distilled, it yields an oily liquid, known as *oil of tar*, and a solid, black residue, *pitch*. It is freely soluble in alcohol, ether, and the fixed and volatile oils, and also to a slight extent in water.

PHYSIOLOGICAL ACTION.—As tar contains a notable proportion of creasote, if taken in sufficient quantity it is capable of exerting the peculiar influence of that agent upon the system. But creasote is not the only active principle in it: hence tar differs from that drug in acting more than it does upon the mucous membranes. That tar is capable of acting as a poison is shown by the case reported by Taylor (*Principles and Practice of*

Medical Jurisprudence, 2d ed., vol. i. p. 334), in which death resulted in a man from taking by mistake the *oil* of tar. To cause death, tar itself would have to be ingested in enormous quantity, since a sailor (according to Stillé) is said to have recovered after taking between a pint and a quart of it.

Applied to any part, tar acts as a very decided stimulant.

THERAPEUTICS.—Tar is used internally almost solely as a stimulant expectorant in the advanced stages of obstinate *acute bronchitis*, or in chronic *bronchitis*. Its chief use in medicine is in chronic diseases of the skin, as a stimulant application in the form of the officinal *ointment* (*Unguentum Picis Liquidæ*, U. S.,—equal parts). In many cases this is too severe, and the strength must be reduced. Prof. Hebra states, in his work on diseases of the skin, that if it be applied too freely enough of the tar may be absorbed to darken the color of the fæces and the urine, and even to cause gastric irritation and black vomit. *Tar Water* may be used internally, in doses of half a fluidounce to one fluidounce; a better preparation is the *Syrup of Tar* (*Syrupus Picis Liquidæ*—6 to 100, U. S.),—dose, half a fluidounce.

CLASS VI.—EMMENAGOGUES.

Emmenagogues are medicines which are employed to promote the menstrual flux. As the stoppage, scantiness, or non-appearance of this secretion arises from very different causes, and as these causes are of diverse or even opposite natures, and may often be removed by drugs, it is obvious that very many remedies of very different character are indirect emmenagogues. Thus, amenorrhœa may depend upon plethora, or it may be the result of anæmia; and whilst in the one case depletory medicines are indicated, in the other case tonics are no less essential. Besides these indirect emmenagogues, there are other substances which appear to act directly as stimulants to the uterine mucous membrane; and indeed it is probable that many of the indirect emmenagogues possess more or less of this power. The emmenagogues may be conveniently arranged in three groups: the tonic emmenagogues, the purgative emmenagogues, and the stimulant emmenagogues.

TONIC EMMENAGOGUES.

Iron is the most prominent member of this section of the emmenagogues. By far the larger number of cases of *amenorrhœa* are associated with, if not dependent upon, anæmia, and are benefited by the use of iron. It should be given in full tonic doses until the anæmia is relieved or the powerlessness of the remedy to effect such change is demonstrated. It is very rarely proper to rely solely upon the iron, which in the great majority of instances should be combined with more decidedly active emmenagogues.

Myrrh has some reputation as a tonic emmenagogue, but, as it is always employed in combination with other more active medicines of its class, the rôle it plays is somewhat uncertain. It should be employed in atonic uterine conditions, and is said to be especially valuable when chronic pulmonary complications exist. The preparations of it most used in amenorrhœa are the compound pills of iron, the compound mixture of iron, and the pills of aloes and myrrh.

PURGATIVE EMMENAGOGUES.

Aloes is believed by some to act as an emmenagogue solely by virtue of its stimulant action upon the rectum, but it very probably directly affects the uterine mucous membrane. Be this as it may, it is a stimulant emmenagogue, especially useful when *atonic amenorrhœa* exists with constipation. Ordinarily it should be given in repeated doses (three times a day) of such size as will produce daily one or two soft, semi-liquid stools. At the menstrual period advantage may be sometimes derived from the administration of a full purgative dose. It is almost always given in combination, especially with iron, whose tendency to constipation it obviates. In *plethoric amenorrhœa*, when torpidity of the bowels is present, salines, and not aloetic purgatives, should be employed.

Black Hellebore has been used by some as a purgative emmenagogue, but is now very rarely if ever employed. From twenty drops to a fluidrachm of the tincture may be given three times a day.

STIMULATING EMMENAGOGUES.

With the exception of guaiac, of parsley, and of one drug of animal origin, the medicines of this class depend upon a volatile oil for their virtue, and are very closely allied in their physiological and therapeutic action.

SABINA—SAVINE. U.S.

The dried tops of Juniperus Sabina, a juniper, native of the south of Europe and the Levant, but very similar to our native species, the Juniperus Virginiana, or red cedar. The active principle is a pale or dark yellow, when highly rectified colorless, volatile oil, which has a strong terebinthinate odor and burning taste, and is officinal (*Oleum Sabinæ*).

The oil of savine is a powerful local stimulant, causing burning and redness when applied to the skin, and is capable of producing fatal gastro-intestinal inflammation. Taken internally in minute doses, its effects are confined to a sense of warmth, with perhaps some ill feeling in the stomach, and slight acceleration of the pulse. After larger amounts, the arterial excitement is more pronounced, and is accompanied by an increased frequency of urination, and sometimes, also, by an actually increased flow of urine. The symptoms induced by poisonous doses are: severe abdominal pain; incessant vomiting and bloody purging; diminution or even suppression of the urine, which is often albuminous and bloody; disordered respiration; symptoms of disturbed innervation, such as unconsciousness, stertorous breathing, convulsions or convulsive tremblings; the scene closing by death in collapse. In pregnant females, abortion, accompanied by violent flooding, almost always occurs before the fatal issue. After death, signs of gastro-intestinal inflammation are generally present, but in some instances these are wanting, and in one case reported by Dr. Letheby (*London Lancet*, 1845) pulmonary apoplexy and congestion of the brain were the chief lesions. Taken in small, repeated doses, savine is a powerful stimulant to the uterine system, and may be used as such in atonic *amenorrhœa*. Its powers in *menorrhagia* dependent upon a relaxed state of the uterine tissues are even more pronounced. Its use as an *abortifacient* is accompanied by the gravest dangers to life. In uterine disease of a sthenic type savine is strongly contra-indicated. The dose of the *oil* (*Oleum Sabinæ*, U. S.), the only preparation which should be used, is from five to ten drops, repeated every three or four hours.

RUTA—RUE.

The leaves of Ruta graveolens, or common garden rue, an undershrub of the south of Europe. Rue has a strong peculiar odor, a warm, bitter, acrid taste, and is dependent for its medical properties upon a peculiar volatile oil, although it also contains a crystalline neutral body, *Rutin*.

The influence of rue upon the system is similar to, but less decided than, that of savine. Locally it is an irritant, producing, when applied to the skin persistently or in a concentrated form, such as the oil, burning, redness, and vesication. According to M. Hélie, taken internally, in large doses, it causes violent gastric pains, excessive and sometimes bloody vomiting, profuse salivation and swelling of the tongue, great prostration, confusion of mind, and convulsive twitchings, with, in pregnant women, abortion. Rue has been, and probably still is, employed in Europe for the production of criminal abortion, and, although its use for this purpose certainly endangers life, I have met with no record of a fatal case. Indeed, the only death from rue that I am cognizant of occurred in a man weakened by dysentery (case, Dr. G. F. Cooper, *Med. Examiner*, N. S., ix. 720). Like savine, it is employed both in *amenorrhœa* and in *menorrhagia* when dependent upon uterine atony; and especial advantage has been claimed for the combination of it with savine. Owing to the aromatic properties of its oil, it has been used somewhat as a *carminative*. The oil, the only proper preparation, may be used in doses of from three to six drops every three or four hours.

PETROSELINUM—PARSLEY.

The root of the Petroselinum sativum, or common parsley. It contains a peculiar, non-nitrogenous, liquid, neutral principle, *Apiol*, which resembles somewhat the fixed oils, but is not saponifiable; a glucoside, *apiin*, and a volatile oil.

PHYSIOLOGICAL ACTION.—The volatile oil of parsley has probably the same physiological and therapeutic value as the more ordinary essential oils, and according to Mitscherlich very large quantities of it (half an ounce) will produce death in the rabbit, largely, no doubt, owing to its local irritant action. The chief interest of parsley to the physician centres in apiol. According to the discoverers of this principle, MM. Joret and Homolle (*Journal de Pharmacie*, 3e série, xxviii. 219), one gramme of it will produce in man a cerebral excitation very similar to that induced by coffee, without other symptoms. In doses of from two to four grammes it causes a species of intoxication, with vertigo, ringing in the ears, and severe frontal headache, —a group of symptoms very similar to those seen in cinchonization.

THERAPEUTICS.—Apiol was introduced by its discoverers as a remedy in intermittent fever, over which, they asserted, it exercised a control secondary only to that of quinia. A commission of the Paris Society of Pharmacy reported that it would cure about half the cases of quotidian and tertian, but was powerless against the quartan; also, that a return of the paroxysm was more common after apiol than after quinia. Clinical experience subsequent to these experiments has, I think, demonstrated that the drug has some power over *malarial disease*, but is very inferior to quinia. In one or two cases in which the latter could not be employed on account of the idiosyncrasies of the patient, I have used apiol very successfully. Joret and Homolle also employed the drug in *intermittent neuralgia*, and in *amenorrhœa* as well as in *dysmenorrhœa*. Joret (*Bulletin Thérap.*, Feb. 1860) has recommended apiol very highly in the last two affections, and his results have been confirmed by Marotte (*Ibid.*, t. lvi., 1863) and other writers. When there was very decided plethora, the apiol was thought by Marotte not to be so efficacious as at other times. In any case of amenorrhœa dependent upon or associated with anæmia or other systemic vice, the continuous administration of iron, tonics, or other suitable medicines must not be neglected. The apiol is given not between the menstrual periods, but just before the latter. Joret and Homolle believe that small doses (three grains twice a day) of it should be exhibited for the week preceding the expected return of menstruation. If any symptoms of the menstrual molimen appear, fifteen grains of it may be administered in the course of a few hours; or they may be given daily for two or three days at the expected time. In intermittent fever, the same quantity may be exhibited four or five hours before the expected paroxysm. On account of its exceedingly disagreeable taste, apiol is always administered in capsules, one of which, as imported from France, usually contains the fourth of a gramme (gr. 3.9).

CANTHARIDES is a very decided uterine stimulant, and is much used as an ingredient of emmenagogue mixtures. From three to five drops of the tincture may be given three times a day; if no unpleasant symptoms arise, the dose may be cautiously increased to eight drops, the production of strangury being of course sedulously avoided.

GUAIAC, as an emmenagogue, is much less stimulating than cantharides, and is believed by some to be especially useful in *rheumatic dysmenorrhœa.* In this affection, full doses of the ammoniated tincture should be given. The following formula, adapted from one of Prof. Dewees, and known as *Dewees's Emmenagogue Mixture*, I rely upon almost exclusively in the treatment of simple atonic *amenorrhœa.* The proportion of the various ingredients should be varied to suit the exigencies of individual cases. Thus, the amount of iron should be altered according to the extent of the anæmia; of the aloes, according to the state of the bowels; of the cantharides according to the susceptibility of the urinary organs:

℞ Tincturæ ferri chloridi, fʒiii; tincturæ cantharidis, fʒi; tincturæ aloës, f℥ss; tincturæ guaiaci ammoniatæ, f℥iss; syrupi, q. s. ad f℥vi. S.—Tablespoonful three times a day.

Tanacetum, U. S.—The common tansy of the gardens in the form of decoction, or of its volatile oil, is sometimes used as a stimulant emmenagogue or for the purpose of producing abortion, but is a very unsafe remedy. When taken in sufficient amount it causes abdominal pain, vomiting, loss of consciousness, and violent epileptiform convulsions.* The minimum fatal dose of the oil of tansy which will cause death is not known, but in two cases (*Cincinnati Lancet and Clinic*, 1881) a teaspoonful of the oil produced violent epileptiform convulsions, and the same amount is said to have caused death (*U. S. Disp.*). Recovery has occurred after one and a half fluidrachms (*Lond. Med. Rec.*, 1882, p. 48). The action of the oil upon the lower animals has been studied by Prof. Guillery (*Bull. Acad. Roy. Méd. Bruxelles*, 1878, xii.). In frogs the most important effects which he found it to produce were paralysis of the peripheral endings of the motor nerves, with early appearance of post-mortem rigidity; paralysis of the vasomotor centre of the medulla, and of the inhibitory cardiac apparatus, with at last paralysis of the heart itself. In warm-blooded animals the oil produced symptoms precisely similar to those it causes in man. After section of the spinal cord the convulsions did not occur in the hind legs, and are therefore of cerebral origin. The arterial pressure was not affected until death was at hand, so that it is evident the drug has little action upon the heart.

Oil of Pennyroyal.—The oil of *Mentha pulegium* is sometimes used as a stimulating emmenagogue in domestic practice, but has very little power. Two fluidrachms taken by a young lady produced vertigo, faintness, muscular weakness, frequent feeble pulse, cold skin and extremities (Dr. C. A. Bryce, *South. Clinic*, vi. 323).

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* For references to fatal cases, most of which have occurred in the United States, see *U. S. Dispensatory*, also Prof. Guillery (*loc. cit.*). Prof. Guillery believes that the symptoms caused by the oil and by tansy tea are different. In a case of poisoning by the leaves, however, reported in the *Nashville Med. and Surg. Journ.*, 1879, xxiii., the symptoms were those alleged to be characteristic of oil-poisoning, and the oil probably is the only active principle of the drug.

CLASS VII.–OXYTOCICS.

Oxytocics are those remedies which are employed during or directly after parturition, to increase the uterine action. It has been asserted that the sulphate of quinia is a member of this class; but, as this subject has been already fully discussed, no more will be here said about it. The power of stimulating the uterine pains has been claimed for various drugs, but at present there is only one substance really used for this purpose; and instead of discussing under the general heading the indications for and the dangers attending the employment of oxytocics, I shall do it in the article upon Ergot.

ERGOTA—ERGOT. U.S.

Ergot is a blackish body, one to two inches in length, irregularly cylindrical, grooved along one side, and very generally curved. When examined under the microscope, it is seen to be composed of very thick-walled cells, which contain oil-drops but no starch. Various opinions have been advanced in regard to the nature of this body; but as by the researches of Tulasne (*Annales Scien. Natur.*, *Botan.*, 3e série, t. xx., 1853) it has been determined exactly what it is, I shall not occupy space with a discussion of the older views. Among the lowest of vegetable organisms, and distinguished from all other plants by the absence of chlorophyl, are the fungi. There are in most cases two distinct states or stages in the life of a fungus: in the first of these, the vegetative period, it exists as a *mycelium*, a usually filamentous mass or flocculus, whose sole function is to grow and increase; in the second stage the *thallus*, or ordinary fungus or mushroom, is formed, and to it is assigned the function of developing reproductive bodies, after whose formation it perishes. Between these stages there is in some fungi an intermediate one, in which the plant exists as a *sclerotium*. The genus Claviceps comprises a number of parasitic fungi, which develop in the pistils of the various species of Gramineæ. The officinal ergot is the sclerotium of the Claviceps (C. purpurea, Tulasne) which infests the grain of the Secale cereale, or rye. The first appearance of the fungus is during the earliest life of the pistil, at the base of which there arises a minute flocculent mass of mycelial filaments. These filaments, continually growing and invading all parts of the tissue of the pistil, at last form of it an irregular whitish body, at the base of which after a time appears a dark-colored body, the sclerotium, which continues to grow, lifting up the diseased and withering mass formed out of the original pistil, and finally developing into a perfect ergot. If a fresh, living ergot be placed in a damp, warm place, after a time little cracks will appear in its surface, and through these cracks little round bodies will project, and finally be raised up on stalks and constitute perfect thalli,—minute fungi, which finally produce spores.

Ergot is an exceedingly complex substance, containing nearly thirty-five per cent. (Legrip) of an inert fixed oil, and, in minute amount, a peculiar ammoniacal base, which was stated by Winckler to be *propylamia*, but appears really to be *trimethylamin*. What its activity depends upon is unsettled, every chemist who has studied it arriving at a diverse result. Three alkaloids have been described from it; two non-crystallizable, *Ecbolina* and *Ergotina*, by Winckler (*Amer. Journ. Pharm.*, May, 1864), and one crystallizable, *Ergotinine*, by Tauret (*Bull. Thérap.*, xciii., p. 231); three acids, *Ergotic*, *Phosphoric* (Levi, *Lo Sperimentale*, Aug. 1875), and *Sclerotinic* (Dragendorff and Podwissotzky, *Arch. Exper. Path. und Pharmak.*, Bd. vi., 192); also various other substances of even still more doubtful nature.[*] As pretty much all are agreed that the watery extract contains all the active ingredients, it may be used as the nearest approach to the active principle at our command.

Physiological Action.—In ordinary therapeutic doses, ergot causes no immediate perceptible symptoms; but when a sufficient amount is exhibited, it acts as a poison both upon man and animals. Before considering its action when given in small quantity, I shall discuss the toxic effects of the drug.

According to Diez (quoted by Stillé), the principal effects of poisonous doses of ergot are in the lower animals profuse salivation, vomiting, dilatation of the pupils, hurried breathing, frequent pulse, cries, trembling, staggering, paraplegia, sometimes diarrhœa, sometimes constipation, prostration, urgent thirst, convulsions,[†] and death. Mr. Saml. A. Wright, in a series of

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[*] Besides papers quoted, the reader desirous of following up the subject should look at Haudelin (*Schmidt's Jahrbücher*, Bd. clv.; T. C. Hermann (*Büchner's Repertorium für Pharm.*, 1871; Bucheim (*Arch. Exper. Pathol. u. Pharmak.*, Bd. iii.; also *Berlin. Klin. Wochens.*, 1876, p. 309; Salkowski (*Berl. Klin. Wochensch.*, 1876, p. 22); Zweifel (*Arch. f. Exper. Path. u. Pharm.*, Bd. iv.).

[†] Pereira (*Materia Medica*, 3d American edition, vol. ii. p. 137), on the authority of Phoebus, states that in the experiments of Diez convulsions were not present.

Sclerotinic Acid.—Dr. Max Stumpf (*Deutsch. Arch. Klin. Med.*, xxiv. 417) asserts that in various hemorrhages he has obtained from the hypodermic use of sclerotinic acid most happy results, but Dr. Rennerb (*Centralb. für Gynecologie*, 1879) has met with nothing but failure. Dr. W. Nikitin (*Würzburger Phys. Med. Verhand*, xiii.) has studied the physiological action of the acid upon frogs, cats, and rabbits. I have seen the report only in abstract, but it is stated that the fatal dose for rabbits was fifteen grains; that directly after the injection the bodily temperature fell from 1° to 3°, and that there was a progressive lowering of muscular power and arterial pressure, and, finally, death from failure of respiration. The paralysis was found to be spinal, and when pregnancy existed contractions of experiments (*Edinburgh Med. and Surg. Journ.*, Oct. 1839, vol. lii.), noted, when the medicine was given by the mouth, symptoms similar to those just spoken of: the paralysis was much more marked than the spasms. Late in the poisoning, the heart's action became irregular and intermittent, and the pulsations, which had been rapid, grew slow and feeble. In some cases the special senses seemed to be destroyed, and coldness of the surface was a very prominent symptom. Mr. Wright also injected a strong infusion of the drug directly into the torrent of the circulation. Death was in some cases produced in nine minutes, the symptoms being immediate dilatation of the pupils, great increase in the rate of the cardiac pulsations, paralysis, and convulsions. When the fatal result was not brought about in so short a space, great anæsthesia of the surface was noted a considerable time before death; coldness of the surface and paralysis of the special senses were also present in some cases. In Dr. Kersch's experiments (*Betz's Memorabilien*, vol. xviii.*) the concentrated infusion was injected into the jugular vein; the coldness of the surface was especially noted, and also great muscular rigidity. Upon rabbits, according to the researches of Wright, ergot acts very feebly. In birds, as represented by chickens, turkeys, and pigeons, it causes symptoms analogous to those produced in mammals, as is testified to by Tessier and by Gross, both quoted by Stillé, and by Bonjean (*Traité de l'Ergot de Seigle*, Paris, 1845). Enormous doses of ergot are required to produce toxic symptoms in animals, since in one of Wright's experiments an amount equivalent to two drachms for every pound weight of the dog failed to kill.

Upon man the toxic influence of ergot is also very slight, and, although I have given the fluid extract in ounce doses, I have never seen it cause any distinct symptoms.† Fatal abortion has several times been produced by ergot; but I know of but two instances of decided poisoning in a non-pregnant person. In the first case (*U. S. Dispensatory*) gastric irritation, thirst, diarrhœa, burning pain in the feet, and convulsions are said to have preceded death. In the second case (Dr. G. S. Oldright, *Canada Med. Journ.*, 1870, p. 404), two hours after taking the drug (amount not stated) there were developed tingling in the fingers and feet, cramps in the legs, arms, and chest, with dizziness and weakness; the pupils were dilated, the pulse was very small, and a feeling of coldness was complained of. These symptoms

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the gravid womb were produced. On the other hand, a series of experiments at the laboratory of the University of Pennsylvania made by Dr. Chas. M. Seltzer with imported sclerotinic acid, showed that this acid at least did not at all represent ergot, and at present it does not seem probable that sclerotinic acid will prove of practical value.

* Unfortunately, I have not had access to Kersch's paper, and know it only by abstracts in *The Medical Times of Canada*, vol. i., and *Schmidt's Jahrbücher*, Bd. clx. p. 120.

† For cases, see Neubert, *Journ. für Pharmacodynamik*, Bd. ii. p. 483, 1860, also, same case, Richter, *Caspar's Vierteljahrschrift*, Bd. xx. p. 177; Tardieu, *Ann. d'Hyg.*, 1855, vol. i.; *Toledo Med. and Surg. Journ.*, July, 1878.

were relieved by the administration of stimulants and the use of external heat; after a time they recurred with greater violence; finally, under the reinstitution of the measures previously employed, the face became intensely congested and purplish red, pain in the head was felt, the patient seemed much excited,* and convulsions were feared, but did not occur; there was some diarrhœa, with dark-gray stools. In the case recorded by Neubert (*loc. cit.*), the great coldness of the surface was especially noted; and as this symptom was very prominent in the case recorded in the *Toledo Medical and Surgical Journal*, and has been so commonly remarked in ergotized animals, it probably is characteristic of poisoning by the drug. Dr. Davidson reports a case with fluid blood, jaundice, and universal hemorrhages, attributed with doubtful correctness to poisoning by ergot (*London Lancet*, ii. 1882, p. 526).

The above summary of the general symptoms caused by poisonous doses of ergot shows that the phenomena are mainly paralytic in their nature; but, although an enormous amount has been written about the drug, we have very little knowledge as to the immediate causes of the paralysis. Since both Wright (*loc. cit.*, pp. 320, 321) and Köhler have found that the voluntary muscles are not affected by ergot, it would seem that the nervous system must bear the brunt of the poison. Eugene Haudelin is said to have shown that the peripheral nerves are not affected,† and the experiments of Köhler have confirmed this so far as concerns the motor nerves and the watery extract of ergot. He found, however, that those portions of the drug not soluble in water appeared to increase the excitability of the peripheral efferent nerves, and that upon the peripheral sensory nerves both portions of the ergot acted as a feeble depressant. On the whole, it is probable that the chief action of the drug is upon the nerve-centres.

The chief interest to the therapeutist in regard to the physiological action of ergot centres upon its influence on the circulation, especially on the blood-vessels, and upon its action on the impregnated uterus. I shall discuss these points *seriatim*. Before doing so, it would be, perhaps, best to speak of the chronic poisoning by ergot; but, as any deductions from the symptoms of ergotism as to the physiological action of the drug would be at best only inferences, I shall defer the consideration of the subject to the section on toxicology.

Action on the circulation.—Although the heart is profoundly affected in acute poisoning by ergot, yet death is probably not due to this cause, since Wright (*loc. cit.*, p. 320) found that after death, even though the heart was quiet, it commenced to beat so soon as the congestion was relieved by an incision, and continued to pulsate for fifteen minutes.

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* These symptoms were very probably caused by the large quantities of alcohol taken.

† *Inaug. Dissert.*, Dorpat, 1871. I have seen only an abstract, contained in *Schmidt's Jahrbücher*, Bd. civ. p. 142.

One of the earliest careful cardiac studies of ergot is that of P. Eberty (abstracted, *Schmidt's Jahrbücher*, Bd. clviii. p. 127). He found that in the frog the injection of a gramme of ergotin caused a diastolic arrest of the heart, and that the viscus was unable to respond at all to stimuli. It is inconceivable that this can be due to other than a direct action of the drug upon the cardiac muscle; yet Eberty seems to believe it is caused by an influence exerted through the pneumogastrics, and it is said that after division of these nerves even very great quantities of ergotin are powerless to produce cardiac arrest.

In man, full doses of ergot unquestionably diminish the frequency of the pulse, since the phenomenon has been independently noted by Parola, Gibbon, Arnal, Hardy, Beatty (all quoted by Prof. Stillé), and by Profs. Bailly and Sée (*Bulletin Thérap.*, t. lxxviii. p. 435); but the method in which this reduction is brought about is uncertain. The amount of the reduction varies from ten to thirty-five beats per minute; but very rarely is the pulse reduced below sixty even by the largest doses. According to Eberty's experiments, therapeutic doses of the drug produce in mammals, as in man, slowing of the heart's beat. It was found that in frogs the pulsations of the heart were still affected after destruction of the medulla, but that in mammals, after paralysis of the peripheral vagi by atropia, ergot was powerless to alter the cardiac rhythm. These experiments, if correct, appear to prove that ergot acts as a stimulant to the peripheral cardiac nerves, and that the reduction of the number of beats is due to this, and is independent of the nerve-centres. Boreischa has noticed that toxic doses quicken the heart's action, and that under these circumstances galvanization of the par vagum has little or no effect upon the heart. It would seem, therefore, as if the drug first stimulated and then paralyzed the peripheral pneumogastrics.

As early as 1827, M. Courhant advanced the opinion that ergot produces a spasm of the blood-vessels; but, although his theory was very generally adopted, only within a very few years has any earnest attempt been made to prove or disprove its correctness. In 1870, Dr. Ch. L. Holmes (*Archives de Physiol.*, t. iii., 1870) found that when the blood-vessels of the frog's web were watched under the microscope and the animal poisoned either with the aqueous extract of ergot or with the powdered drug, the vessels, both venous and arterial, could be seen to undergo a very great contraction. Dr. A. Wernich (*Virchow's Archiv*, 1872, Bd. lvi. p. 510) observed that when rabbits in which the arteries of the thigh, back, pia mater, etc., were exposed, received full doses of ergot, these arteries could be seen to undergo a very remarkable diminution in their calibre. These observations have been confirmed by other observers, among whom may be mentioned Vogt, Dr. S. Kersch (*loc. cit.*), Max. Schüller (*Berliner Klin. Wochensch.*, 1874, p. 305), and Boldt (*Schmidt's Jahrbücher*, March, 1872). The latter observer also affirms that there ran through the ergotized capillaries wave-like, peristaltic spasms. Patrick Nicol and J. Mossop (*Brit. and For*

Medico-Chir. Rev., vol. l., 1872) have noted with the ophthalmoscope the contraction of the retinal vessels after the exhibition of ergot in man.

If general vaso-motor spasm be produced by ergot, unless the heart's action be greatly weakened by the drug there must be a very decided rise in the arterial pressure. The question as to the existence of this rise was first investigated by Dr. Ch. L. Holmes (*loc. cit.*). This experimenter injected the aqueous extract directly into the jugular vein of the dog, whilst the manometer or the kymographion was connected with one of the main arteries. The phenomena induced were immediate, rapid, and very decided depression of the arterial pressure, with violent cries and efforts on the part of the dog, followed by a period of quiet and a rise of the arterial pressure above the normal point. Twenty-three experiments were performed: in two of them the first depression of the arterial pressure was wanting; in six of them the arterial pressure did not rise above normal. As the experiments are not reported in detail, it is not possible to point out in all the cases the causes of these exceptional phenomena; but Dr. Holmes mentions sickness of the animal, death during the stage of depression, or some other obvious reason for the departure from the usual results, as being present in nearly all the cases, so that the exceptions are, I think, at present best disregarded in the interpretation of the phenomena. As Köhler and Eberty (*Virchow's Archiv*, Bd. lx. p. 384) and myself have all found that ergotin (Bonjean's) raises the arterial pressure enormously in frogs and mammals, the fact must be accepted as proven.

Dr. Holmes tried the effect of the injection of the ergot after section of the cardiac nerves, but obtained results so varying and contradictory that he could come to no other conclusion than that the alterations of the arterial pressure produced by ergot are not dependent upon its cardiac action. In the absence of details of these experiments, we can but accept this conclusion.

The unexpected result in the investigation of Dr. Holmes was the primary depression of the arterial pressure, a depression which at first sight seems incompatible with the idea that ergot contracts the vessels. It is, of course, possible that the fall of pressure may be due to an intense action of the drug upon the heart; but Dr. Holmes, in order to explain it, propounds a theory which is very plausible, but which he certainly does not prove to be true. His idea is that the first fall of the arterial pressure is due to a spasm of the pulmonic capillaries, hindering the blood in its passage to the left heart, and thereby causing venous repletion and arterial depletion. It is to be remembered that he injected the ergot directly into the jugular vein, so that the whole force of the remedy fell directly upon the pulmonic circulation. It is evident that this matters very little if ergot produces vaso-motor spasm only through an influence upon the nerve-centres, but that it does make a material difference if the contraction of the vessels be the result of a local action. Holmes asserts that after section of a sympathetic nerve and injection of the ergot the vessels supplied by the divided nerve can be seen to contract; and Wernich confirms this observation. If ergot does thus cause vaso-motor spasm, it is plain that in Dr. Holmes's experiments this spasm must have been very intense in the lungs before the systemic capillaries were affected. Our investigator proved by experiment what *a priori* seems necessarily true, that if blood be prevented from passing freely to the lungs the arterial pressure falls very greatly. In this connection it is worthy of notice that the period of arterial depression following the injection of the drug into the jugular vein was very brief. In the only experiment detailed in full by Dr. Holmes, the pressure began to rise in three minutes after the completion of the injection; in five minutes it was nearly normal, and in eleven minutes it was above the normal point. If the asserted facts are all true, the theory of Dr. Holmes is plausible. It is, however, very doubtful whether the ergotic spasm is local in its origin. Evidence derived from judging by the eye as to whether a vessel does or does not contract must be taken *cum grano salis*, and the observations of Holmes, of Wernich, and of J. H. Peton (*De l'Action Physiol. et Thérap. de l'Ergot*, Paris, 1878) are directly contradicted by the apparently careful and elaborate experiments of Dr. Paul Vogt (*Berliner Klin. Wochenschr.*, 1869, No. xii.), in which the dilated vessels of the ear of a rabbit whose cervical ganglion had been extirpated could not be made to contract by ergot.*

The results obtained by P. Eberty (*Inaug. Dissert.*, Halle, 1873) are in accord with those of Vogt, and disagree with those of Dr. Holmes, especially in their bearing upon the question whether the contraction of the arteries is centric or peripheric in its origin. He finds that the arterial pressure rises directly and enormously after the injection of ergotin. This rise, which he acknowledges to be chiefly due to the contraction of the vessels, occurs in the veins as well as in the arteries, and in the frog as well as in the dog and the rabbit. According to his experiments, it must be, at least in the batrachian, centric, since in the frog it does not take place after destruction of the medulla. He also found that after the inhalation of nitrite of amyl the ergot caused rise of the arterial pressure. It is a fair inference that if the vaso-motor spasm be centric in the frog it is also so in the mammal.

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* In a series of experiments made by Prof. S. Ringer and Dr. H. Sainsbury (*Brit. Med.*, Jan. 1884) upon tortoises according to the method of Gaskell (see *Digitalis*, p. 150), the addition of ergotin greatly slowed the rate of flow through the arterioles.

These results certainly appear to be contrary to the previous drift of our evidence in showing that ergot acts locally upon the vessels. It was found, however, that the addition of ergotin to the saline solution used had no distinct effect until there was ten per cent. of the extract in solution. Ten per cent. of ergotin is enough very seriously to influence the viscidity of the saline solution, and it is probable that the slowing effect of the ergotin was the result of altered physical conditions; a conclusion which is corroborated by the fact that the records clearly show complete loss of vitality in all parts of the tortoise experimented with, a loss of vitality which in all probability was shared by the arteries. Certainly these experiments cannot be accepted as valid in contradiction of the older results.

In an especial investigation (*Phila. Med. Times*, vol. iv.) of the subject, I found that ergotin injected into a vein does, as Holmes states, produce in the mammal an immediate fall of the arterial pressure, which is shortly followed by an enormous rise. I also found that division of the cord, *i.e.*, vaso-motor paralysis, does in dogs prevent the rise of the pressure, and hence that the latter is centric, due to a vaso-motor spasm. As the vaso-motor action of the drug must now be acknowledged as centric, the theory of Holmes falls. If this be true, the only conceivable cause of the first fall of pressure must be a direct action on the cardiac muscle, upon which the ergotin is at once precipitated when thrown into the jugular vein. That this is the real cause I think is demonstrated by the facts that the fall does not occur when the drug is introduced gradually into the circulation by hypodermic injection, and that the drug is a poison to the cardiac muscle, as was shown in my experiments as well as in those of Eberty.

Haudelin is stated to have found that the arterial pressure falls after the exhibition of the poison. Brown-Séquard has insisted (*Archives de Physiologie*, 1870, t. iii. p. 434) that in ergotic poisoning there are two periods: first, vaso-motor spasm; second, vaso-motor paralysis, and Haudelin noted a fall of arterial pressure after toxic doses. Dr. Boreischa (*Arbeiten. Pharm. Laborat., Moskau*, i. 55) also, in a number of experiments, using Bonjean's ergotin, found a very decided fall of pressure produced by the drug. In none of these experiments was there any rise of pressure at all; either the ergotin used was not equivalent to that employed by Holmes and myself, or else the result obtained was dependent upon the use of very large doses. In a series of experiments, Boreischa found that the fall of pressure after section of the spinal cord high up was proportionately not nearly so great as in the normal animal. This indicates that the fall of pressure was due to vaso-motor palsy. It would seem, therefore, that the conclusions of Brown-Séquard are correct, and that decidedly toxic doses of ergot lower the arterial pressure, by depressing both the heart and vaso-motor centres.

Action on the intestines.—The fibres in the coats of the blood-vessels are certainly not the only non-striated muscles upon which ergot acts: indeed, the probabilities are strong that the drug influences muscular fibre of this character wherever it exists in the body. There is considerable evidence to show that it causes increased intestinal peristalsis. In Dr. Wright's experiments (*loc. cit.*, p. 320) the intestines were found in very active peristalsis at the post-mortem examination of the poisoned animal. Dr. Wernich (*Virchow's Archiv*, 1872, Bd. lvi. p. 515) noticed that very violent peristaltic movements followed the injection of ergot, as was seen not only in rabbits whose abdomens were opened, but in some cases even through the uninjured walls; and Haudelin has confirmed his observations.

Uterus.—Upon the uterus of parturient women ergot exerts a very pronounced and fixed influence, increasing the length and force of the pains, and, if it be given in sufficient dose, causing after a time violent tetanic cramp of the whole organ. The drug certainly acts in this respect upon the lower animals as it does upon man, since Youatt states that in a large experience, both with monogastric animals and ruminants, he has never known the drug to fail in its action on the uterus of the parturient female.

The action of ergot in producing contraction in the impregnated but not parturient womb is by no means so constant. Upon animals, Dr. Wright found it to fail in all of a number of trials, as did also Bonjean in a single experiment. On the other hand, Diez (Stillé, *Therapeutics*, 2d ed., vol. ii. p. 585), Oslere (*Ibid.*), and Percy and Laurent (*Ibid.*) found it to cause abortion in guinea-pigs, sows, rabbits, cows, and cats; and M. Bodin has reported an epidemic of abortion occurring among cows near Trois Croix, which he attributes to feeding upon ergotized grasses (*Journal des Connaissances Médicales*, 1842). The evidence of those who have used ergot for the induction of premature labor in woman tallies very closely with that which is brought forward in regard to the lower animals. As the matter is so fixed, I will not enter into an elaborate discussion of the effects of ergot upon pregnant women. To show that the fungus very often will act as an abortifacient, it is only necessary to quote Prof. Ramsbotham, who states (*The Principles and Practice of Obstetric Medicine and Surgery*, Phila., 1860, p. 318) that he has made a "great number of trials," and found that "expulsive action soon followed its exhibition, with very few exceptions." It cannot be gainsaid, however, that very often the drug has failed: sometimes, no doubt, because of poor quality or because given in insufficient dose, yet sufficiently often to show that its abortifacient action is uncertain.*

Whether the uterine disturbance is of centric origin, or is due to a direct action of the drug upon the uterus and its nerve-fibres, is uncertain, although the drift of the present evidence is towards a peripheral action. Dr. Wernich, in two experiments, found that no vermicular movements were produced in the unimpregnated womb by ergot after section of the spinal cord; but in one of these experiments the animal was so feeble as to destroy any possible force the result might have, and I do not think much weight is to be attached to the evidence. On the other hand, Boreischa, in several experiments, succeeded in producing violent uterine movements after dividing all of the nervous connections of the organ.

THERAPEUTICS.—As a therapeutic agent, ergot is employed both by the obstetrician and by the physician; and I shall consider these uses of it separately.

Owing to the power that ergot possesses of intensifying labor-pains, it has been long used in *uterine inertia* during parturition. Indeed, it was for this purpose that the drug was first employed in medicine, and thereby acquired the name of *pulvis parturiens.* The literature of the subject is immense, and all imaginable opinions as to the effects of the drug when given in labor, and as to the advisability of its employment, have been advanced; but, without discussing these, I shall here simply point out the clearly-established rules for its use and the clinically-determined dangers and advantages of its employment. If ergot be given in very small doses during labor, the natural pains are simply intensified; but if the dose be large enough to have a decided effect, their character is altered: they become not only more severe, but much more prolonged than normal, and finally the intervals of relaxation appear to be completely abolished and the intermittent expulsive efforts are changed into one violent, continuous strain. It is evident that, if the resistance be sufficiently great, this may endanger the safety both of the mother and of the child. The dangers to the mother are twofold: there is a possibility of the uterus rupturing itself by its efforts; and, when the head comes down upon the perineum, if the soft parts be rigid there is a very strong probability that they will be lacerated. The danger of uterine rupture is, I think, a remote one; for although several alleged cases have been recorded, yet in very few is the accident clearly traceable to the asserted cause (see Stillé, *Therapeutics*, 2d ed., vol. ii. p. 591). The fatal character of the accident is such, however, that the possibility of its occurrence should always prevent the reckless use of the drug.

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* For a more elaborate setting-forth of the matter, the reader may consult Prof. Taylor's *Principles and Practice of Medical Jurisprudence*, 2d ed., 1873, vol. ii. p. 193.

The improper use of ergot is far more serious in its effects upon the child than upon the mother. During a violent uterine contraction, the passage of the blood from the placenta to the child must be interfered with, or, in other words, the respiration of the fœtus is temporarily stopped, so that its life depends upon the aeration of the blood during the intervals. If the latter be very much shortened, the life of the child is greatly imperilled; and if they be abolished, it must be destroyed, unless delivery occurs in a very few moments. These considerations are, I think, sufficient, without further discussion, to show the imperativeness of the rule *never* to give ergot in uterine inertia when there is much *resistance*, either in the bony or in the soft parts of the mother. In primiparæ such resistance is always to be looked for, and its degree often difficult to judge of beforehand; and in such women ergot should not be used at all for the purposes of expulsion. Even under the most favorable circumstances for its employment—when the woman has previously borne children, when the bony pelvis is capacious, and the soft parts are relaxed and dilatable—its use should be entered upon with caution; and if the accoucheur be skilful in the application of instruments, cases must be rare in which the latter are not preferable to the ecbolic.

In women of lax fibre, with roomy pelves, ergot may be used in uterine inertia if instruments are not at hand, or if they are objected to, or if the obstetrician is timid in their application.

At the close of parturition, ergot is very commonly employed to prevent *post-partum hemorrhage;* and in this case there is no objection to its use, and the remedy is invaluable. But, as it requires from fifteen to twenty minutes for its action when given by the mouth, ergot exhibited in this way cannot be relied upon to arrest flooding when it has already set in. To prevent the occurrence of the latter, it is an excellent rule to give a full dose of the ecbolic when the child's head is well down upon the perineum and beginning to emerge at the vulva. After labor, if a tendency to bleeding is manifested, the exhibition of ergot may be added to the other measures employed. Its hypodermic use under these circumstances would be eminently proper.

For the induction of *premature labor*, ergot has been and still is to some extent used; but it is uncertain in its action, and offers no advantages over instrumental methods.

The success of ergot in arresting hemorrhage after labor soon led to its use in uterine hemorrhages in other than parturient or pregnant women; and the next step beyond this was its employment in other hemorrhages. In all forms of *hemorrhage* in which no direct local application can be made, ergot is to-day probably the most generally used remedy; and even when local applications can be made, if the bleeding be obstinate, ergot is very generally exhibited. It is thus employed in *menorrhagia*, in *hæmoptysis*, *hemorrhage* from the *gums*, *epistaxis*, etc., etc. Ergot acts with especial rapidity and efficiency in these cases, if given hypodermically: used in this way, the suddenness of the result in hæmoptysis is sometimes surprising. Even when the hemorrhage is apparently dependent upon a dyscrasia, as in *purpura hæmorrhagica*, the hypodermic injections of ergotin sometimes produce the happiest results (cases, *Brit. Med. Journ.*, ii., 1874; *Philad. Med. Times*, vol. v.). The value of the drug in hemorrhage is no doubt dependent upon its power of contracting the small vessels. In colliquative *night-sweats* due to relaxation of the blood-vessels, ergot is a most efficient remedy.

Allied to its use in hemorrhage is the employment of ergot in *enlargement* of the *spleen* from various causes. Dr. Da Costa was the first to suggest hypodermic injections of the drug for this purpose, and he claims to have even cured *leukæmia* (*Amer. Journ. Med. Sci.*, Jan. 1875).

It was the physiological action of ergot upon the muscular fibres in the walls of the vessels that led Prof. Langenbeck to try the effect of the hypodermic injection of the remedy in *aneurism*. The result obtained, as reported in the *Berliner Klin. Wochensch.* (vi., 1869), was surprising. How far surgeons have followed up this matter I do not know; but, according to Dr. Paul Vogt (*Berliner Klin. Wochensch.*, March, 1872), Schneider has cured a case of femoral aneurism, and Dutoit one of the subclavian. Vogt has himself employed the remedy successfully in a very severe case of varicose veins of the legs, of many years' standing. The remedy is injected into the immediate neighborhood of the aneurism or varix, one or two grains of ergotin, or the aqueous extract of ergot dissolved in water and a little alcohol, being employed every day. A good deal of local swelling and hardness is induced, and it is certainly a question whether the good achieved has not been simply the result of the local inflammation set up.

Very many years ago, Dr. F. E. Barlan-Fontayral proposed (*Journ. des Sci. méd. pratiques de Montpellier*, tomes vi., vii.) the use of ergot in *chronic dysentery* and *diarrhœa*, on account of its power of causing contraction of the capillaries; and Massolaz, in an epidemic of chronic diarrhoea among the French troops serving in the Orient, found that the suggestion was well timed. Although Barlan-Fontayral afterwards published a book (*Le Seigle ergoté et de l'Application de l'Ergotine à la Cure de la Dysentérie et de la Diarrhée chroniques*, Montpellier, 1858) upon the subject, yet it attracted little or no attention. In 1871, Prof. A. Luton, of Rheims (*Gaz. Hebdomad.*, Oct.), stated, as something new; that he had used ergot with remarkable success in a violent and protracted epidemic of *dysentery*. Successful cases of *chronic diarrhœa* are also reported by other observers (see *Schmidt's Jahrbücher*, Dec. 1871; *Lancet*, 1876, ii., p. 409), so that trials of the remedy should be made in all obstinate cases.

Another employment of ergot for the purpose of restraining excessive secretion is in *galactorrhœa*, in which affection it has been used with success by Dr. Le Gendre (*Bull. Thérap.*, t. lxxvii. p. 282) who was led to employ it by an observation of Drs. Poyet and Commarmond (*Annal. de la Soc. de Méd. de Saint-Etienne et de la Loire*, 1863) that wet-nurses fed upon ergotized bread lost their milk.

The use of ergot in diseases of the nervous system has recently attracted a good deal of attention. It would appear to be especially indicated in congestion of the nerve-centres, and in *congestion* of the *cord* has been especially commended by Brown-Séquard, Hammond, Beard, and others. I have employed it with most excellent results in numerous cases, and there can be no doubt as to its great value when given in sufficiently large doses. In other diseases of the nervous system its use is not so clearly established. Dr. Hampel (*Practitioner*, vol. i. p. 263) recommends it in *whooping-cough*. Mr. Woakes believes the pain of *neuralgia* (*Ibid.*, p. 257) to be due to congestion and serous effusion into the nerve-sheaths, and has used ergot with very good results. Dr. Daniel H. Kitchen (*Amer. Journ. of Insan.*, July, 1873) has employed it with great success in *headaches* of the most diverse and even opposite origins, and has cured (?) *epilepsy* with it. In the latter disease he continues its use for months.

In 1872 (*Berliner Klin. Wochensch.*, June 17), Prof. Hildebrandt announced that in nine cases of *fibroid tumors* of the uterus he had used with the utmost advantage hypodermic injections of ergotin; and this practice has been followed very widely on this continent. It is scarcely to be doubted that cures are sometimes effected, but probably in the majority of cases* the drug simply lessens the uterine congestion, and does good precisely as it does in *chronic subacute metritis* and in *subinvolution* and *hypertrophy* of the *uterus* (Meadows, *Practitioner*, vol. i. p. 166); it may be that sometimes it strangles the growth by causing uterine contractions. If the latter be the case, a cure, as is suggested by Prof. Goodell (*Proceed. Med. Soc. of Pennsylvania*, 1873), is to be expected from the remedy only in mural and submucoid tumors.

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* See *Amer. Journ. Med. Sci.*, July, 1873; *Amer. Practitioner*, May, 1873, May, 1874, August, 1874; the *Clinic*, April, 1873; the *Lancet*, May, 1873; *Chicago Med. Journ.*, 1874; and especially Dr. Byford's Address, *Trans. of Amer. Med. Assoc.*, 1875.

An objection to the method of Hildebrandt is the great pain and local inflammation which often result; and Goodell proposes, as a substitute, the use of enemata or suppositories containing the drug.

Very recently, led by a fancied resemblance between the physiological action of ergot and that of quinine, Dr. Duboué has proposed the fungus as a succedaneum to the alkaloid in *malarial fevers*, and in support of his views has published a book entitled *Recherches sur les Propriétés thérapeutiques du Seigle ergoté*, Paris, 1873. He brings forward some evidence of the value of the remedy; but probably the latter will share the fate of the older substitutes for the South American specific. Dr. Th. Clemens (*Deutsches Klinik*, 1865, p. 267) affirms that ergot affords the most potent relief in the *ammoniacal cystorrhœa* of paraplegics. He gives it internally, but especially uses injections into the bladder of a solution of ergotin (gr. ii to f℥v). Ergotin suppositories are asserted to be of great value in *hemorrhoids* (*N. Y. Med. Record*, xvi. 563). I have used them in one or two cases without benefit.

Toxicology.—Enough has already been said in regard to the acute poisoning by ergot, except it be to state that, when abortion is threatened from its ingestion, in the maintenance of perfect quiet and in the free exhibition of opium are to be found all the measures of relief at our command.

Since the days of Galen, there have swept over larger or smaller districts of Europe epidemics of diseases which have been attributed to ergot. In many parts of Europe, rye bread forms the great staple article of food of the lower classes. It always contains a small quantity of ergot, but not enough to have any deleterious effect upon the health. When the summer is wet and cold, the rye becomes very extensively ergotized, so that the fungus constitutes a large proportion of the materials entering into the bread. It is under these circumstances that there occur those epidemics of *ergotism* or chronic ergotic poisoning which have been recorded from time to time since the days of Galen and of Cæsar. It is not always the rye which causes these frightful losses of life, as Heusinger (*Journ. für Pharmacodyn.*, Bd. i. p. 405) has traced one epidemic to diseased oats. Before going farther, it seems proper to state that no less an authority than Trousseau and Pidoux asserts that these epidemics are not dependent upon any specific action of ergot, but are either epidemics of blood-diseases or simply the results of improper and insufficient food,—merely the outcomes of poverty, wretchedness, and famine. It seems to me indisputable that some of the various epidemics which have been recorded were of this character, but certainly it is no less indisputable that others were not. Moreover, quite numerous scattered cases are on record in which a few persons or a family have been affected with ergotism unmistakably traceable to the use of bread largely composed of the fungus.*

The scope of the present work is such as to forbid my entering into an elaborate discussion of the epidemics of ergotism, especially as the subject has no practical bearing so far as the American profession is concerned, since the absence of deep poverty is so complete in our country that no one would feed on largely ergotized bread, and, in fact, no case of ergotism has as yet been recorded as occurring in the United States.†

There are two varieties of ergotism, the spasmodic and the gangrenous.

Gangrenous ergôtism has been especially observed in France, and is believed to be the same as the *Ignis Sacer* or the *Ignis Sancti Antonii* of the Middle Ages,—an affection which in 922 killed forty thousand persons in Southwestern France, and in 1128–29 fourteen thousand in Paris alone. It generally commences with itching and formications in the feet, severe pain in the back, contractions in the muscles, nausea, giddiness, apathy, with abortion in pregnant women, in suckling women drying of the milk, and in maidens amenorrhœa. After some time, deep, heavy, aching pains in the limbs, an intense feeling of coldness with real coldness of the surface, deep apathy, and a sense of utter weariness, develop themselves. Then a dark-red spot appears on the nose or on one of the extremities; all sensation is lost in the affected part; the skin, perhaps over a large surface, assumes a livid red hue, and in the foci of local changes bullæ filled with serum appear. The adynamic symptoms, in severe cases, deepen as the gangrene spreads, until finally death puts an end to the scene. Very generally the appetite and digestion are preserved to the last, and not rarely there is an almost ferocious hunger. The gangrene is generally dry, the parts withering and mummifying; but sometimes it is moist, and pyæmic symptoms may even be developed. Of course a very large number of cases do not terminate in death; but the part immediately affected is generally lost. In these cases the toes most generally are the portion destroyed, but it may be any one or all of the extremities; and the nose, lips, ears, and even the buttocks, sometimes bear the brunt of the disorder.

Spasmodic ergotism may in the lightest cases be manifested only by itchings, formications, numbness, or complete anæsthesia of the fingers and toes or of the buttocks, and by gastro-intestinal irritation, as shown by colic, vomiting, diarrhœa, or constipation, and withal a ravenous hunger. In more severe cases these manifestations are intensified, and spasmodic symptoms appear, violent and painful tonic contractions affecting especially the flexors of the extremities, interrupted at times by intervals of quiet, but gradually growing into severe general tetanic paroxysms, with opisthotonos and emprosthotonos. In the intervals there are very generally muscular tremblings, and as the case progresses there are developed cerebral manifestations, such as disturbances of vision, photophobia, chromopsis, hemiopia, and periodic amblyopia and amaurosis, giddiness, cataleptic and epileptic paroxysms with or without loss of consciousness, delirium, and idiocy. Gastro-intestinal symptoms are always very marked, but with them is a characteristic ravenous hunger and a longing for sour food and drink. The skin is earthy or yellowish in its tint, often spotted with boils or pustules or semi-gangrenous vesicles. Death is apparently caused by exhaustion; and in those that recover, various local paralyses, habitual spasms, amaurosis, mental aberrations, or even idiocy, often remain through life. In a few cases the symptoms are still more violent, and the spinal and cerebral disturbances soon lead to death.

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* For a modern epidemic, see *Deutsch. Arch. f. Klin. Med.*, xxxiii. 246.

† Any one especially interested in the subject will find the literature very well represented in the references of Prof. Stillé's work on Therapeutics, to which may be added Duboué's book, quoted on the previous page. For the reader of German, a very excellent résumé exists in Husemann's *Handbuch der Toxicologie.*

In some epidemics of ergotism the cases have been a mixture of the spasmodic and gangrenous forms of the disease.

ADMINISTRATION.—Ergot may be given in powder, but at present this method is very rarely used: the dose is half a drachm to two drachms. The U. S. Pharmacopœia recognizes a *wine* (*Vinum Ergotæ*,—1 to 6.6) and a *fluid extract* (*Extractum Ergotæ Fluidum*). The first of these is a good preparation for internal use, and may be administered, as an ecbolic, in doses of half an ounce to two ounces. The fluid extract is, however, preferable. The usual ecbolic dose is one to two drachms. In nervous diseases much larger doses are required: thus, in congestion of the spinal cord I usually commence with half an ounce, and increase it to an ounce three times a day.* Of the so-called *Ergotin* two varieties have been proposed, that of Bonjean and that of Wiggers. Bonjean's ergotin is made by exhausting the ergot with water, evaporating to the consistency of a syrup, precipitating the albumen, gum, etc., with an excess of alcohol, decanting the clear liquid, and evaporating to the consistency of a soft extract. This ergotin is believed to be about ten or eleven times as strong as ergot, five or six grains of it representing about a drachm of the drug.

The ergotin of Wiggers simply contains everything in the ergot which is insoluble in water. Köhler (*Virchow's Archiv*, Bd. lx.) has proved that Wiggers's preparation has no influence upon the circulation, but in toxic doses produces violent convulsions. It ought not to be employed therapeutically. Bonjean's ergotin is that usually kept in our pharmacies, and represents all the virtues of the remedy. The officinal *extract of ergot* (*Extractum Ergotæ*, U.S.) is probably as good for hypodermic use as Bonjean's ergotin, and in all respects represents the drug therapeutically. Its strength is five times that of the fluid extract; when used hypodermically it should be dissolved in water and filtered. It is stated that the danger of severe local trouble is much lessened by plunging the nozzle of the syringe deeply into the muscular tissues. In an elaborate research (*Du Bois Reymond's Archiv.*, 1884, 434) upon the activities of the various derivatives from ergot, M. Marckwald found that the *ergotinin preparations* (*Ergotinum Citricum* of Gehe, *Ergotinum Solutum* of Bombelon) raise the arterial pressure, whilst *sclerotinic* acid depresses it; and the *ergotin* (*aqueous extract*) first raised, then depressed, then raised the arterial pressure; also that the ergotin and sclerotinic acid act violently upon the uterus, whilst the ergotinin preparations do not influence the organ.

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* It would appear that sometimes, owing to idiosyncrasies, even small amounts of ergot cause much disturbance. Thus, Dr. R. B. Faulkner reports (*New York Med. Journ.*, June 14, 1884) a case in which a fluidrachm of the fluid extract caused great sleepiness, swelling and redness of the feet, and violent prickling of the extremities.

GOSSYPII RADICIS CORTEX, U. S.—The root of the ordinary cotton-plant is asserted to be used by the negroes in various portions of the South as an *abortifacient*, and Dr. Bouchelle, as long ago as 1841, claimed for it medical properties similar to those of ergot. It has not, however, come into general use, and our knowledge of its properties is at present very scanty and uncertain. In the experiments of Dr. I. C. Martin enormous doses produced heaviness and stupor both in frogs and mammals, but did not cause abortion in pregnant guinea-pigs and rabbits: neither the spinal cord, the muscles, nor the nerves were affected (*Amer. Journ. Med. Sci.*, Jan. 1882). The oxytocic dose of a decoction (℥iv in a quart of water boiled to a pint) is stated to be a wineglassful, to be repeated every thirty minutes as necessary. The remedy has also been employed in *amenorrhœa* and in *dysmenorrhœa*, in which diseases from three to five grains of a solid aqueous extract have been given three times a day. The *fluid extract* (*Extractum Gossypii Radicis Fluidum*, U. S.) may be used in doses of a fluidrachm.

The *Smut of Indian Corn* (*Ustilago*, U. S.) appears to have active medicinal properties, and should be investigated. It has been used successfully in *uterine inertia* during labor by Dujardin-Beaumetz (*Bull. Thérap.*, xciii. 85). Consult also *N. Y. Med. Journ.*, xxiv. 654; *Schmidt's Jahrbücher*, Bd. 172, p. 19; *Centralb. für Med. Wiss.*, 1876, p. 228; *Chicago Med. Times*, 1879–80, xi. 434. Dr. James Mitchell has found that in the frog the ustilago maidis abolishes sensation and reflex action before voluntary motion; he states that reflex action is destroyed at a time when motor nerves and muscles are still active, and that consequently the first influence of the poison is upon the sensory side of the lower nervous system; late in the poisoning the whole motor tract became involved (*Unpublished Inaug. Dissert.*, 1883, University of Pennsylvania).

CLASS VIII.—SIALAGOGUES.

SIALAGOGUES are medicines which increase the flow of saliva and of the buccal mucus. Various substances, such as mercury, when taken internally, affect the mouth and its tributary glands in such a way as to produce salivation: these substances are, however, never employed in medicine for this purpose, so that practically sialagogues are local remedies acting by the induction of a local impression on the mouth. The influence which they exert is a stimulant one, and most of them are more or less irritant. They are used to effect two distinct purposes. Some of them dissolved in the saliva pass over the mucous membranes not only of the mouth but also of the fauces and of the epiglottis, and exert upon them a direct stimulant influence. Other sialagogues, by exciting a very great flow of saliva, seem to lessen the congestion of the part.

In reference to the first of these modes of action, sialagogues are employed in relaxed conditions of the mucous membrane of the fauces, and even of the larynx. Chief among the substances so used is cubebs, which when slowly chewed in the mouth exerts a very decided local influence, and is useful in relaxation of the fauces, of the uvula, and even of the upper portions of the larynx. Either in form of the berries or made into lozenges, cubebs is much used by public speakers; and in the *hoarseness* from relaxation following over-use or slight inflammation, it is often very efficient.

Through their depletory influence, sialagogues are sometimes useful in allaying *rheumatic toothache*, or other rheumatic irritations about the jaws. The only remedy of the class employed for the purpose and requiring a separate notice here is pellitory.

PYRETHRUM, or *Pellitory*, is the product of the Anacyclus Pyrethrum, a small herbaceous perennial, growing in the neighborhood of the Mediterranean. It is a small root, about the size of the little finger, wrinkled longitudinally, light brown externally, with bright, shining spots on the surface, hard, brittle, with a resinoid radiated fracture. It is inodorous, and when chewed is at first almost tasteless, but soon becomes acidulous, saline, and acrid, and produces a very persistent burning, tingling sensation, which is accompanied by a profuse flow of saliva. Half a drachm to one drachm of it may be chewed at a time in painful *rheumatic affections* of the face, in *toothache*, in *relaxation* of the *uvula*, and in similar disorders. Taken internally in excess, it acts as a narcotic irritant, fifty minims of its tincture having caused gastro-intestinal irritation, with violent convulsions, which nearly proved fatal in a child three and a half years old (*London Practitioner*, xvii., p. 86.)

CLASS IX.—ERRHINES.

THESE are substances employed to act upon the mucous membrane of the nose. Strictly speaking, the term should be applied only to those drugs which are used to excite secretion in the nasal mucous membrane. Such remedies are, however, so rarely used as to be by themselves scarcely worthy of notice. The employment of irritating vapors to arouse the nerve-centres by stimulating the nerves distributed in the nasal mucous membrane, is a very old and a very popular custom. *Smelling-salts*, or preparations of hartshorn, so much used by ladies as a slight stimulant, and by others in reviving those who are suffering from or threatened with fainting, act in this manner. The ammonia held close to the nostrils brings about the reaction, not by any direct stimulating action on the circulation, but by irritating the nasal mucous membrane, as is proven by the rapidity of its influence and by the exceedingly minute quantity which will sometimes act efficiently. In the use of hartshorn, especially with young children, it is necessary to exercise care, lest injury should be done to the delicate mucous membrane. The only errhine used for the purpose of influencing affections of the nasal passages themselves which is worthy of mention here is *cubebs*. This freely snuffed up in powder is very useful in *acute coryza*, after the first stage of congestion and dryness has passed away.

CLASS X.—EPISPASTICS.

Counter-irritation.—Almost from time immemorial, physicians have believed that morbid processes in deep-seated or superficial organs could be modified by irritations artificially induced in distant parts. To the drugs used for producing these remedial irritations the name of revulsives or counter-irritants has been given, the process being called revulsion, or counter-irritation. Latterly, the value of these remedies in disease has been questioned, chiefly because not only were the accepted theories of their action deemed untrue, but any explanation of how they do what is claimed for them was asserted to be, in the present state of our knowledge, inconceivable.

Evidently, in studying the matter, the inquiry should be divided into two parts, and fact should be separated from theory; the effort being made to ascertain, first, whether experience does or does not demonstrate that it is possible by an irritation to affect a distant part which has no apparent connection with the seat of the new irritation; second, whether the facts taught by experience are in truth irreconcilable with reason. In regard to the first part of this inquiry, it seems to me indisputable that experience does teach, in the most unequivocal manner, that an organ may be affected through a distant part. There are physiological proofs of this, which it is only necessary to allude to: such is the relation of the uterus and the mammary glands. The proofs which may be drawn from disease are, however, much more numerous and striking. Thus, it is well known that in mumps there may be relief of an existing irritation of the salivary gland by a new irritation of the testes; in gout, the swelling of the toe will relieve the disordered digestion, etc. If it be affirmed that these phenomena, happening during the existence of a blood-disease, are *sui generis*, the objection cannot be made to the paraplegia produced by the irritation of a calculus in the kidney, or to the headache due to the irritation of the gastric mucous membrane by acid, or to the shoulder-pain of diseased liver, or to the amaurosis caused by the irritation of a decayed tooth. A well-known experiment of Brown-Séquard's illustrates the point so well that it may be quoted. In it he found that if one sciatic nerve of a guinea-pig be cut, epileptic attacks may be produced by gently rubbing the back of the ear upon the same side. A very curious instance of an external irritation affecting a deep-seated part is the duodenal ulcer produced by burns, especially of the abdomen. The pathological evidence of the truth of the present proposition is simply overwhelming, and facts might be brought forward almost indefinitely to show that irritations are capable of affecting the functions and nutrition of distant parts. This being true, surely it is in the highest degree reasonable to suppose that artificial irritations can in a greater or less measure be controlled so as to affect the distant organ for good and not for evil.

Clinical experience has certainly demonstrated that this can be done. The va'ue of any individual counter-irritant in this or that disease is not the present question; but certainly no physician who has had any practice can have failed to see instances of relief from the use of counter-irritants. A case of obscure brain-trouble recalls itself at present writing, in which stupor and a clear intellect alternated at will, according as the drastic cathartic was given or withheld. The relief of abdominal pain, or "stomach-ache," by a mustard plaster, is a daily nursery experience.

From what has been already stated, it may be laid down as proven beyond cavil—first, that we have power to influence internal morbid processes by creating external irritations; second, that the fact of counter-irritation exists, whether we can or cannot explain its rationale.

Physiological knowledge is not yet sufficiently extensive to enable us to perfect a theory of counter-irritation. The action of these remedies is complex, but I think can be explained at least in part. There is only a certain amount of blood in the body. If it be accumulated in one place, it cannot be in another. Thus, the difficulty of studying after a hearty dinner probably depends, as do the cold feet so common in feeble persons under such circumstances, upon the accumulation of blood, and probably also of nervous energy, in the digestive organs. Now, by artificial interference, by determined study, by violent exercise, we can often draw the blood away from the alimentary apparatus into the cerebrum, or into the motor system, and produce indigestion. Clinical experience proves that we can also reverse this process. The brain is excited, the blood is concentrated in it, congestion exists, inflammation is threatened; a drastic cathartic is given, the blood is drawn into the intestinal canal, and by revulsion the brain is relieved. Certainly this is not mysterious, not inexplicable. All forms of counter-irritation cannot, however, be explained on the above principle. It is a probable, but not a positive, teaching of modern physiology that there are nerves which preside over nutrition,—the so-called trophic nerves. If this be so, it is to be expected, *a priori*, that peripheral irritations will cause reflex alterations of nutrition, precisely as they cause reflex disturbances of the motor functions. Further, whether these trophic nerves do or do not exist, there are vaso-motor nerves, and the duodenal ulcer of burns is a positive proof that, either through the trophic or through the vaso-motor nerves, external irritations do produce internal reflex alterations of nutrition. The sympathetic ophthalmia caused by a morbid eye in its healthy fellow, or induced by a diseased tooth, is another instance of this reflex alteration of nutrition.* As this is true, it seems to me absurd to state that it is impossible to conceive how an external counter-irritant can affect the nutrition of a deep-seated organ.

It is evident that in all the cases which have been mentioned of external irritation causing disease in a distant organ, there is no direct communication between the part irritated and the organ which is secondarily affected. And clinical experience confirms the evident deduction from this,—*i.e.*, that it is impossible to determine, except by experiment, where the counter-irritant should be placed to affect most powerfully any given organ. It has, however, been clinically demonstrated that the general law for deep-seated parts is that the revulsant should be put directly over the part. When a superficial action is desired, other directions are needed. We are indebted to Dr. Anstie for pointing out what appears to be another law,—namely, that when a superficial part supplied by the anterior branches of a spinal nerve is to be affected, the counter-irritant should be placed over the posterior roots of the nerve. Not only can obstinate neuralgia often be relieved by this reflex action, but also the inflammatory changes so often coincident with intercostal neuralgia. The law seems also to apply to cervical nerves, since the proper position for the blister in facial trigeminal neuralgia is back of the ear or on the nape of the neck. Dr. A. Dumontpallier affirms that the best results of counter-irritation are obtained by applying the counter-irritant upon the opposite side of the body, so as to be exactly symmetrical with the pain, and especially commends hypodermic injection of water as a counter-irritant (*Gaz. Hebdomadaire*, Nov. 14, 1879).

Counter-irritants may be conveniently arranged under two heads: 1st, those which produce a decided structural alteration of the skin, including *epispastics;* 2d, those which do not provoke decided alterations of dermal structure, the *rubefacients.* The indications for the use of these substances can best be considered under their respective headings.

As is well known, any sthenic inflammation, if of sufficient extent and intensity, may excite the general system even to the point of high fever. In this respect inflammation of the skin does not differ from that of other organs. Hence dermal irritants have a direct tendency to arouse or excite the system, and may be used as general stimulants. It will be seen at once that it is the nervous and arterial systems which alone feel their influence. Hence the irritants should not be relied upon in cases of exhaustion, for the only possible source of absolute increase of power to the system is in food; and in exhaustion those stimulants should be employed which increase the power of assimilating food. For this reason, external irritants are useful as stimulants in conditions of depression rather than of exhaustion. Such conditions of depression exist in *acute collapse* from any cause, in "*shock*" following injuries, in the first stage of *pernicious malarial fever*, in *snake-bite*, and in other cases when the powers of the system are seemingly overwhelmed by some depressing agency. The rubefacients are preferable to blisters for this purpose, because their local after-effects are comparatively so trifling that they can without injury be applied to a very large extent of the surface.

EPISPASTICS, *vesicatories*, or, more colloquially, *blisters*, are substances which are used by the physician to produce that peculiar inflammation of the cuticle and outpouring of serum known as a blister. The immediate effect of a blister is more severe and more permanent than that of a rubefacient. Blisters are especially useful in inflammations of serous membranes, such as *pleuritis* and *peritonitis;* are very strongly recommended by some practitioners in parenchymatous inflammations, such as *pneumonia;* and are often of service in *neuralgia*, and in other forms of nervous irritation, such as the *maniacal delirium* of fevers, when dependent upon the irritant action of a blood-poison, and not upon exhaustion. The amount of serum which is poured out from a blister is sometimes quite large, and vesicants have even been used to relieve *dropsy*. In general dropsy, their use is simply unjustifiable; but in *local dropsies*, as, for example, serous effusion into the pleural sac or into the pericardium, dependent upon local disease, they often do good, not only by affecting favorably the disease-process, but also by hastening the removal of the effusion.

In some chronic affections, long-continued severe counter-irritation is required: in such cases a blister may be "kept open" by the use of stimulating ointments, such as the unguentum mezerei. In *chronic inflammation* of the *joints*, repeated blistering is very often of service. When the inflammatory action is rheumatic, in my experience better results are obtained by repeated blistering than by keeping a blister sore by means of irritants. In *neuritis*, whether rheumatic or otherwise, blisters are often of service: they should be applied as a long narrow strip along the course of the nerve. In obstinate local *neuralgia*, very mild blistering over the seat of pain, or in accordance with Anstie's law, is sometimes advantageous.

The *contra-indications* to the use of blisters are high arterial and febrile excitement and a decided want of vital power. In the former case, the irritating influence which they exert upon the general system may increase the constitutional disturbance to such an extent as to do far more injury than any local benefit derived from them can do good. When the vitality is very weak, blisters may give rise to sloughing ulcers, which, refusing to heal, may waste very seriously the already exhausted system. Hence, in all acute diseases of such type that the nutritive forces are exceedingly depressed, blisters must be avoided, or must only be used with great caution. For the same reason, great care must be exercised in their employment in the very young or the very aged. Very rarely indeed is a blister called for in the case of a young infant, and, when employed, it should be allowed to remain in contact with the skin only just long enough to produce slight redness, and the complete vesication should be obtained by the use of the poultice.

There are various substances which are capable of producing vesication, but the only one in ordinary use is cantharides. In cases of emergency, a blister, it is said, may be raised in a very few minutes by the use of the *stronger water of ammonia*, a little of which is to be kept in contact with the skin by means of an inverted watch-glass. It is necessary to watch the process closely, and to remove the irritant so soon as vesication has occurred, as the ammonia is very capable of causing sloughing.

CANTHARIS—CANTHARIDES. U.S.

The dried bodies of the Cantharis vesicatoria, a beetle inhabiting Southern Europe, and coming into commerce in Spain, Italy, Sicily, and the southern provinces of Russia. *Spanish flies* are from half an inch to nearly an inch in length, and two to three lines in breadth, and have a large heart-shaped head, and brilliant metallic-green elytra or wing-cases. Their odor during life is very strong and fetid, but is almost entirely lost in drying; their taste is urinous, very burning, and acrid. They are taken in May and June, when they swarm on the trees which they affect, by beating the branches early in the morning, when the insects are torpid from the cold, catching them upon linen sheets, and plunging them into hot vinegar and water, or exposing them to the fumes of boiling vinegar. In some places they are gathered by smoking the trees with the fumes of burning brimstone. When ground, Spanish flies afford a grayish-brown powder, full of minute greenish spangles, the remains of the feet, head, and wing-cases. The active principle of cantharides is *Cantharidin*, which occurs in white crystalline scales, is inodorous, tasteless, insoluble in water, nearly so in cold alcohol; soluble in ether, benzole, the oils, and very freely so in chloroform. Notwithstanding the insolubility of their active principle, Spanish flies yield their virtues to alcohol and to water, because, as is generally believed, a yellow coloring-matter is so united with the cantharidin as to render it soluble.

Physiological Action.—When a minute therapeutic dose of cantharides is taken, no perceptible immediate result is produced, and after a somewhat larger quantity the only symptom is usually some burning and pain in urination. Doses more than just sufficient to induce this should not be employed in medicine, as the symptoms produced by large amounts of the drug are exceedingly severe and distressing. Cantharides is very irritating, and, when applied to the skin, causes at first redness, with burning, then free vesication and severe pain, and, if the contact be longer maintained, deep inflammation and sloughing. Upon the mucous membranes it produces a no less intense effect; and consequently gastro-intestinal inflammation forms a prominent symptom of poisoning by it. Further, the active principle or principles are undoubtedly absorbed and are eliminated by the kidneys, coming in contact with almost the whole genito-urinary mucous membrane: hence intense irritation and inflammation of these organs always result from the ingestion of an overdose of Spanish flies.

Very soon after a toxic dose of cantharides has been taken, the sufferer is seized with burning in the pharynx and œsophagus, and a sense of stricture in the throat. The pain soon spreads to the stomach, and vomiting comes on. The symptoms rapidly increase in severity; the abdominal pain becomes very severe, and, in the majority of cases, purging takes place. The matters rejected by the stomach are first mucous (with, if the drug have been taken in powder, little greenish specks through them), then bilious, and finally bloody. The stools are mucous, then fibrinous, bloody, becoming often very scanty, but excessively numerous, and in their passage accompanied by great tenesmus. Probably in most cases very early in the attack, severe salivation is developed, and is very frequently accompanied by great swelling of the salivary glands. Sometimes death occurs in a very short time, from collapse produced by the intense gastro-intestinal inflammation; but more generally it is postponed for some hours, and a new train of symptoms arises. Aching pains in the back, and very frequent micturition, indicate the commencing urino-genital irritation. These symptoms increase in intensity until there is a constant irresistible desire to urinate, with violent tenesmus of the bladder, and yet an inability to pass more than a few drops of urine, which is albuminous, and not rarely bloody. In some cases there is a violent erotic excitement, an unquenchable lust, accompanied in man by numerous seminal emissions; violent priapism, swelling and heat of the organs, and even severe inflammation of the parts, indicate the intensity of the local action of the poison; sometimes gangrene ultimately occurs.

Neither amatory desire nor true priapism is, however, a constant symptom in cantharidal poisoning (cases, *Journ. de Pharm. et de Chimie*, June, 1871): indeed, the former is probably absent in the majority of cases. Consciousness and general power are often long preserved amid intensely severe local symptoms and agony, but, if the dose have been large enough, sooner or later collapse comes on with its usual symptoms, and the prostration deepens into complete powerlessness, stupor, coma, and finally death. In some cases violent hydrophobic delirium and severe tetanic convulsions are said to have occurred (Tardieu). Paraplegia has been noticed in several cases by Dr. Pallé (*Journ. de Pharm. et de Chimie*, June, 1871): it was probably reflex in its origin, and due to the intense irritation of the urino-genital organs.

In animals, cantharides produces very much the same symptoms as in man. In dogs, according to the experiments of Orfila and of Beaupoil, the symptoms of gastro-intestinal inflammation are more prominent than those of irritation of the genito-urinary tract. It has been asserted that the lack of erotic excitement in these cases shows that the medicine acts differently upon man and animals. As already stated, however, erotic delirium is very generally absent in fatal poisoning by man, whilst Schroff states that ten drops of the tincture of cantharides will frequently produce great sexual excitement in man, and the whole drift of the evidence is that libidinous desires are much more apt to be caused by amounts of Spanish flies but slightly toxic, than by fatal doses. Indeed, the irritation caused by the latter would seem to be too intense, the general perturbation too great, for erotism to be induced. There appears to be the same difference in the effects of different doses of the drug upon animals. Fatal doses very generally do not excite sexual desire, but Schubarth (quoted by Stillé) found that small doses do cause evident salaciousness and irritation of the genital organs, whilst, according to Husemann (*Handbuch der Toxicologie*, 1862, p. 264), the peasants of Northern Germany habitually give cantharides to cows when backward in coming into heat at the proper season. According to Dr. Cautieri (*Schmidt's Jahrb.*, Bd. clxv. p. 237), toxic doses of cantharides rapidly lessen blood-pressure and the force of the cardiac pulsations, but markedly increase the pulse-rate. He found in animals killed with cantharides marked hyperæmia of the brain and spinal cord and very decided nephritis. M. Galippe (*Gaz. Hebdom.*, 1874, p. 439) noted inflammation of the alimentary canal, kidneys, and bladder.

THERAPEUTICS.—Cantharides is employed internally only for the purpose of influencing the genito-urinary organs; and sufficient has already been said in regard to this use under the headings of Diuretics and Emmenagogues. The external use of cantharides is simply as a vesicant; and the employment of blisters has been sufficiently considered in the general discussion of the class. Two points, however, seem worthy of notice here: first, that this drug affords the only practical means of blistering at our command; secondly, that when it is freely employed there is always some danger of the absorption of a sufficient amount of the active principle for strangury to be induced. In susceptible persons, therefore, care has to be exercised in the use of epispastics; and whenever active irritation of the kidneys exists, cantharidal blisters should not on any account be applied.

TOXICOLOGY.—Sufficient has already been said about the symptoms produced by cantharides. The minimum fatal dose is not certainly determined, and probably varies very much. According to Stillé, twenty-four grains of the powder, taken in two doses, have caused fatal abortion, and an ounce of the tincture has destroyed life after the lapse of a fortnight. After death, intense injection, swelling, patches of exudation, loss of epithelium, and other results of inflammation are found along the whole tract of the alimentary canal; intense hyperæmia of the kidneys, with contraction and injection of the bladder, also usually exists. According to the experiments of Aufrecht (*Centralb. f. Med. Wissensch.*, xx. 1882, 850), all the forms of nephritis may be produced by cantharidin in various doses, but it is probable that in most cases of poisoning the first change is exudation of the white blood-corpuscles, rapidly followed by a desquamative nephritis, with profound alteration in the glomerules (see Dr. Ida Eliaschoff, *Virchow's Archiv*, xciv. 323).

There is no known antidote to cantharides, and the treatment of the poisoning must be conducted upon general principles. The stomach, if not already thoroughly emptied, should be evacuated at once by a stimulating emetic if the stomach-pump be not at hand. Large quantities of mucilaginous or albuminous drinks should be taken; and all oily substances should be avoided, as favoring the solution, and consequently the absorption, of the poison. Opium should be freely exhibited, especially by the rectum, to allay pain and relieve the strangury. For the latter purpose warm sitz-baths or general baths should be given. In some cases leeches to the epigastrium are advisable. When the suffering is very intense, the cautious use of anæsthetics seems to me not only justifiable, but imperative. In the stage of prostration, the measures to be adopted are those commonly practiced in collapse from poison.

Administration.—The preparation of cantharides most commonly used for the production of a blister is the *Cantharides Cerate* (*Ceratum Cantharidis*, U. S.), which is best spread upon sticking-plaster in such a way as to leave a margin about an inch in width, which shall adhere to the skin and hold the plaster in its place. The *Cantharides Paper* (*Charta Cantharidis*, U. S.) is thought to be more elegant than the plasters made of the cerate, and is said to be efficient. In order for a blister to "draw" thoroughly, it usually has to be left on some eight hours; but in most cases the same result can be achieved with less suffering by allowing the blister to remain only six hours, or until decided redness and slight vesication have been induced, and then applying a flaxseed poultice. In certain localities vesication requires a much longer application than that just spoken of: thus, upon the shaved scalp a blister will rarely act efficiently in less than twelve hours, and often not in that time. In maniacs, in the delirious sick, in children, and in other unruly patients, it is often necessary to put on a blister in such a way that the sick person has no control over it. For this purpose the *Cantharidal Collodion* (*Collodium cum Cantharide*, U. S.)* may be used. It is ordinary collodion impregnated with cantharides, and on evaporation leaves an adhesive blistering film: two or three coats of it should be applied, by means of a camel's-hair brush. When there is any especial danger to be feared from absorption of the active principle, the use of the poultice, after a brief application of the blister as described above, should always be practiced. The *liniment of cantharides* (*Linimentum Cantharidis*, U. S.) contains turpentine, and is used as a violent rubefacient liniment. The *Ceratum Extracti Cantharidis*, U. S., is probably an efficient blistering preparation, but has not been much tested. The tincture (*Tinctura Cantharidis*, U.S.) is used internally in doses of three to five drops.

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* For case of poisoning by cantharidal collodion, see *Phila. Med. Times*, iv. 312.

CLASS XI.—RUBEFACIENTS.

RUBEFACIENTS are those remedies which are employed for the purpose of producing, not any permanent inflammation of the skin, but a general intense irritation, redness, and congestion, which shall exert a temporary influence, whose power is the result of the large surface affected, and not of any permanent impression upon the nutritive acts of that surface. Most, if not all, rubefacients are capable of causing disorganizing inflammation if allowed to remain for too long a time in contact with the skin.

The superiority of rubefacients over blisters when it is desired to arouse or stimulate the system has already been pointed out (see p. 532). It remains to speak of the use of rubefacients in local diseases. They are especially useful in sudden cases of severe pain due, it may be, to acute congestion of a part, or to some internal irritation like that of gout. Thus, in the ordinary intestinal pain caused by irritant articles of food, or more commonly by a rheumatic, gouty, or other irritation following exposure to cold or wet, rubefacients are most useful. In this as in all other cases of what may be termed temporary functional derangement, when a counter-irritant is desired, rubefacients are superior to blisters, because their effects are not nearly so lasting, and also because, for the time being, they seem to impress more powerfully the nervous system, breaking up, as it were, the concentration of nervous energy, or calling off the irritation, or impressing the nervous system in some way which in our present ignorance it is difficult to find terms to express. A correct idea of the difference in the use of the two classes of counter-irritants can perhaps be conveyed by saying that when profound local alterations of nutrition are to be dealt with, blisters are to be used; when functional disturbance is to be met, rubefacients are to be employed. Yet this rule cannot be applied with strictness.

SINAPIS ALBA—WHITE MUSTARD. U.S.
SINAPIS NIGRA—BLACK MUSTARD. U.S.

The seeds of the Sinapis alba and Sinapis nigra respectively,—European crucifers, cultivated in the temperate regions of the world. These seeds are minute, globular bodies, yellowish within: they are to be distinguished one from the other by the smaller size, external brown color, and more fiery taste of the black mustard, and the light yellowish exterior of the white mustard

Black Mustard contains *Myronic Acid* in combination with potash, and also a peculiar albuminous principle, *Emulsin*. When to these substances water is added, a reaction occurs, resulting in the production of a volatile oil out of the myronic acid. *Volatile oil of mustard* is a colorless or yellowish fluid, of an intensely pungent, or even corrosive, odor and taste. A momentary contact with it suffices to redden and blister the skin, and mucous membranes are said to be rapidly destroyed by its vapors.

White Mustard does not yield on distillation with water a volatile oil, but contains an acrid fixed principle. The chemistry of white mustard seeds appears not to have been certainly determined. In 1825, Henry and Garot discovered a substance in them,—*Sulpho-sinapisin*,—which, according to Husemann, has been variously designated as *Sinapin*, *Sinapisin*, *Sinapinic Acid*, etc., but has been demonstrated by Babo and Hirschbrunn to be an alkaloid, which also exists in the seeds of the black mustard. Robiquet and Boutron believe that the acrid fixed principle of white mustard is formed by a reaction between this and water in the presence of the emulsin.

PHYSIOLOGICAL ACTION.—The oil of mustard is a most intense irritant, and if taken internally would act as a very powerful irritant poison. The ground mustard, of course, shares its properties.

THERAPEUTICS.—Mustard affords a most excellent material for the practice of mild revulsion. One great advantage it possesses is the ease with which it can be controlled,—all grades, from the mildest impression up to severe blistering, being at the will of the practitioner. It should be remembered, however, that the blister produced by it discharges but little, and is exceedingly sore and painful as well as very slow and difficult of healing: so that, as an epispastic, mustard is in every way inferior to cantharides, and should not be employed. The black mustard is much stronger than the white, and must usually be diluted at least one-half (by the addition of flour or of flaxseed meal). The white variety may sometimes be employed pure, but generally it also may be reduced in strength.

In many cases it is desirable to maintain for hours a mild, equable counter irritant impression; and this may be done by adding from one to three teaspoonfuls of mustard, more or less, to a poultice of flaxseed. A mustard poultice half-and-half black mustard, three parts to one white mustard, and flour, may generally be left on from twenty minutes to half an hour without danger of blistering. Weaker preparations may be used longer. A mustard plaster may be prepared like an ordinary poultice; but a very convenient method is to take a newspaper folded to a little larger than the desired size, and tear open the front piece so that it can be folded back like a flap, leaving one edge attached; next, to spread upon the thick portion the mustard, leaving the edges free, and then to close the flap upon it and fold the edges back to the desired shape: when done with, this plaster can be thrown away, and no rags are lost. The mustard draws well through the single layer of newspaper covering it, but is, I think, less apt to leave troublesome after-soreness than when employed in the usual manner. In the 1870 edition of the U. S. Pharmacopœia a new preparation of mustard was introduced, under the name of *Charta Sinapis*, or *Mustard Paper*. It consists of black mustard mixed with solution of gutta-percha and spread upon stiff paper four inches square. These mustard papers may be useful for travelers, but in my experience do not act so well as the home-made mustard plaster. Their size is not so easily regulated, and their action is often too violent.

Capsicum and the *stronger spices* afford excellent materials for rubefaction. The Cayenne pepper is probably as strong as mustard, but is much less pleasant to handle, on account of the readiness with which it is diffused, and is much less frequently employed. *Spice-plasters* are useful when it is desired to make a steady, continuous mild impression, as in certain abdominal complaints. They may be made by the apothecary by means of the following recipe: Take of powdered ginger, ℥ii; powdered cloves and cinnamon, each, ℥i; Cayenne pepper, ʒii; tincture of ginger, f℥ss; honey, q. s.; mix the powders, add the tincture, and sufficient honey to make of proper consistence for a stiff cataplasm. The domestic spice-plasters are much more elegant and cleanly than those made on the above plan. They are to be prepared as follows. Take equal parts of ground ginger, cloves, cinnamon, and allspice, and one-fourth part of Cayenne pepper, and thoroughly mix them; then put the resulting dry powder into a previously-prepared flannel bag of the desired size, distribute the powder equably through the latter, and quilt it in,—*i.e.*, run lines of stitching across the bag, so as to confine the powder in little compartments. When used with common whisky or with alcohol, a plan which has seemed to me still more pleasant is to put two ounces of *unground* ginger, an ounce of unground cloves, cinnamon, and chillies, or African peppers, in a pint bottle, and pour the whisky upon them. After this has stood awhile, the liquor is to be put upon a piece of flannel of the proper size, and the latter is to be laid upon the part and covered with a larger piece of oiled silk, or else a piece of spongio-piline may be employed. If the strength of the preparation is too great, it can readily be reduced by dilution; if it is too little, it can as readily be increased by adding more of the spices, especially of the peppers. In many cases, when the tenderness is very great, the weight of the spice-plaster is objected to. Under these circumstances the substitute here proposed is especially valuable.

Oil of Turpentine is a very powerful rubefacient, capable, if applied to the skin for too long a time, of destroying the epidermis. It produces, when properly used, simply an intense diffused redness. The most frequent mode of application is in the form of *stupes*, which should be made by dipping a piece of flannel, previously wrung out with warm water, into a cup of the turpentine which has been warmed by setting it in hot water, and then wringing out all excess of the turpentine, and applying. These stupes may be left on from ten to thirty minutes, according to the severity of the impression desired and the susceptibility of the patient's skin. On some persons the least contact of turpentine, or even of its vapors, produces a most painful furuncular eruption. Where this idiosyncrasy exists, of course the remedy should never be used. The officinal liniment (*Linimentum Terebinthinæ*, U. S., *Kentish Ointment*) is used as a stimulant application to burns. According to the U. S. Dispensatory, it should be applied as soon as possible after the reception of the burn, by covering the injured surface with pledgets of patent lint saturated with it, and should be allowed to remain on until the peculiar inflammation excited by the fire has subsided.

Ammonia is a most efficient rubefacient, which in its general relations has been sufficiently discussed elsewhere. When great haste is required, it may be employed as an epispastic by applying a piece of common lint, saturated with the strongest water of ammonia, and covering it with some impervious coating. Great care must be practiced lest the ammonia act as an escharotic, since a too prolonged application may produce a deep slough. To raise a blister requires from five to ten minutes. On account of its cheapness and efficiency, ammonia is very largely used in extemporaneous liniments. In prescribing, it must always be borne in mind that there are two waters of ammonia: *Aqua Ammoniæ Fortior*, U. S., with a specific gravity of 0.900, containing twenty-six per cent. of the gas; and *Aqua Ammoniæ*, U. S., with a specific gravity of 0.960, containing about ten per cent. of the gas. The rubefacient action of ammonia is less permanent than that of turpentine. There is an officinal *liniment* (*Linimentum Ammoniæ*, U. S.), containing one part of the simple water to two parts of olive oil. It is, of course, an ammoniacal soap.

PIX BURGUNDICA, U. S., or *Burgundy Pitch*, is a concrete juice obtained by wounding the Abies excelsa, or Norway spruce, and Abies picea, or European silver fir,—lofty forest-trees of Middle and Northern Europe,—melting the product of the exudation with hot water, and straining. It is hard, opaque, brittle, of a feeble terebinthinate odor and taste, and contains resin and a minute amount of volatile oil. It is a mild rubefacient, which, in the form of plaster, may be kept applied for a long time in *chronic bronchitis* and in *rheumatic affections* of the trunkal muscles. The officinal *plaster* (*Emplastrum Picis Burgundicæ*, U. S.) contains one-twelfth of its weight of wax. The *Warming Plaster* (*Emplastrum Picis cum Cantharide*, U. S.) contains one part of cantharides cerate to twelve parts of Burgundy pitch, and is a very decided counter-irritant, whose prolonged use will sometimes blister susceptible skins.

PIX CANADENSIS, U. S., or *Canada Pitch*, is the concrete juice of the Abies Canadensis, or the indigenous hemlock spruce of this country, purified by melting with water and straining. It is hard and brittle in winter, soft in summer, of a yellowish-brown color, deepening to black on exposure. It contains resin and a minute quantity of volatile oil, and is used for the same purpose as the Burgundy pitch. The *plaster* (*Emplastrum Picis Canadensis*, U. S.) contains one-twelfth of its weight of wax.

CLASS XII.—ESCHAROTICS.

Escharotics are drugs which are used to destroy diseased or sound tissue. Many of them exert a purely chemical influence, whilst others seem to destroy life by directly affecting the vitality of the part, and are said to act dynamically. Those which act chemically do so in several ways; some, like bromine, probably produce an intense corrosive oxidation, whilst others, like sulphuric acid, abstract the water.

Escharotics are used for various purposes. Formerly they were employed to open abscesses; but in the very few cases in which the knife is not allowable, as in abscess of the liver, aspiration affords, without doubt, a much superior and, in *hepatic abscess*, much safer method. They are constantly employed to destroy unsound, harmful tissues and growths. Thus, they are used to remove the specific tissue of a *chancre*, or to kill a *malignant* or *semi-malignant tumor*. Another purpose which they fulfil is the destruction of *poisoned wounds*. In these cases they may in some instances destroy the poison itself, but in other cases they simply prevent the absorption of the toxic agent by putting an end to the life-actions of the tissue containing it. It is hardly necessary to mention all the various cases in which caustics are employed to overcome the effects of poisoned wounds. *Hydrophobia* is a perfectly uncontrollable disease; but the thorough destruction of the wounded tissue at any time before the manifestation of the symptoms will probably prevent its occurrence, as it will certainly do if performed early. In *malignant pustule*, life depends upon the free early use of escharotics. Escharotics are employed to produce ulcerations which shall be the bases of *issues;* also, by destroying the exuberant granulations or the indolent surfaces of *ulcers*, to remove at the same time diseased tissue, afford protection to the parts below by forming an impermeable surface, and exert such alterative action upon the part as shall modify for good the life-processes.

It is evident that the choice of the caustic should depend upon the object to be attained. When large tumors are to be killed, or when it is all-important completely to destroy a poisoned wound, a powerful deep-reaching escharotic must be employed; but when the surface of an ulcer is to be filmed over, a caustic which acts superficially and forms a dense albuminous coating, as does nitrate of silver, is to be chosen.

An observation of Drs. N. A. Randolph and S. G. Dixon (*Med. News*, Jan. 4, 1885) indicates that the pain produced by a caustic may be almost nullified by the use of cocaine. They find that the saturated solution of cocaine in nitric acid acts as powerfully although much more slowly than nitric acid, and that the only sensation that is produced during the production of even a deep eschar is a slight prickling.

All of the more powerful of the escharotics, when taken internally in sufficient amount, act as violent corrosive poisons, producing agonizing pain in the œsophagus and hypogastrium, violent bloody vomiting, often purging of similar character, and finally collapse, deepening into death, which is sometimes preceded by convulsions. When the dose is not so large, the system may rally from the immediate effects of the poison to succumb finally to the local lesions produced, or to struggle through a protracted convalescence to health, perhaps only to die years afterwards from organic stricture, caused by the ulcerations of the œsophagus or other of the digestive tubes. The first indication in poisoning by one of these substances is to neutralize or chemically antidote the poison. Many, if not quite all, of the escharotics have some chemical antidote: with the alkalies, dilute acid, generally convenient in the form of vinegar; with the acids, alkalies, generally at hand in the shape of whitewash or of soap; with others, specific substances, which, as antidotes, should be at once exhibited. Opium should always be freely given, and the symptoms during and after the first poisoning be treated as they arise, upon general principles.

POTASSA, U.S.—*Caustic Potash* is officinally prepared by boiling liquor potassæ until ebullition ceases and the potassa melts, when it is run into cylindrical moulds. It occurs in grayish semi-translucent sticks, about three inches long and as thick as a large goose-quill, very deliquescent when exposed to the air, and extremely soluble, except impurities (lime, oxide of iron, and carbonate of potassium), in both water and alcohol. When it is placed upon the skin it soon melts, and, as it does so, gives rise to a pain which increases until it becomes very intense, and continues until the power of the alkali is so lost that it can no longer reach through the tissue it has killed to the sound flesh below. Under the action of the escharotic the skin becomes a dirty ashen-gray, and finally a slough is formed, with inflammation of the surrounding parts, and ulceration and detachment of the dead tissue in from six to ten days. The potash appears to act chiefly by abstracting the water, and, to some extent, by combining with the fatty and other portions of the tissues. Its slough being perfectly permeable, and its power being but slowly expended by its own action, potash is one of the most thorough of the escharotics: it is, therefore, to be preferred when a very deep and decided influence is required, as after the *bite* of a *rabid* dog. It is somewhat uncontrollable in its action, and requires care in its use. The best method of application is as follows. Take a piece of heavy adhesive plaster, and cut a hole in it of such size that, when the piece is warmed and properly placed upon the skin, the part to be acted upon will be exposed whilst all around it will be protected. Then apply the plaster, and grease the outer surface of it, without allowing any of the oil to come in contact with the exposed central skin. Then lay the caustic potash upon the latter, and when the action is believed to have extended deep enough, wash the part with dilute vinegar.

POTASSA CUM CALCE, U. S.—*Vienna Paste* is a grayish-white powder composed of equal amounts of caustic potash and of caustic—*i.e.*, unslaked—lime. It is less active than the simple caustic potash, but is preferred by some on account of its being less apt to spread and diffuse itself. When applied, it is mixed with sufficient alcohol to form a paste, and then used in the manner described when speaking of the simple alkali. M. Piedagnel affirms (*Journal de Pharmacie et de Chimie*, 3e sér., t. xxxiii.) that this caustic may be rendered nearly or entirely painless in its action by mixing one part of the muriate of morphia with three parts of the powder, and then by the addition of chloroform forming a paste that may be spread upon lead-plaster and so applied. In five minutes the skin under the application becomes of a dead white color, and at the end of fifteen minutes is brown and carbonized. If the application be persisted in, the thickness of the eschar becomes finally about equal to that of the layer of the paste employed.

ACIDUM ARSENIOSUM.—As a caustic, *arsenic* is energetic and powerful, but somewhat slow, in its action, and causes intense pain, with violent inflammation of the neighboring parts. It is stated to affect more rapidly morbid than normal structures, and hence is especially used for the destruction of malignant growths. It appears to act chiefly upon the vitality of the part, acting, when sufficiently diluted, as a powerful irritant, and when in a concentrated form producing an irritation so intense that life cannot endure it. Hence, probably, the reason of its affecting more rapidly morbid growths, which, as is well known, have a lower vitality than sound tissues.

The great objection to the employment of arsenic is the possibility of its absorption in sufficient amount to cause constitutional symptoms: even death has resulted from its external use. Absorption takes place, of course, much more rapidly in a healthy than in an intensely inflamed or dead tissue. For this reason, whenever arsenic is employed it should be used freely, and under *no* circumstances should it be applied to a large healthy surface, such as that of a fresh wound. The rationale of these precepts is very evident. Arsenic, if employed at all as an escharotic, must be applied in quantities which would, if absorbed, endanger life; but when a very large amount is used it causes death so rapidly as to prevent absorption. In the case of a fresh wound, the poison may be taken up before it has an opportunity to produce local death.

Used in any way, arsenic is a hazardous caustic, and it ought to be employed only with the knowledge and distinct remembrance of this fact. *Cancer*, and perhaps some forms of semi-malignant ulceration, such as *lupus*, appear to be the only diseases which justify its use. *Sir Astley Cooper's Arsenious Ointment* consists of one drachm of arsenious acid, one drachm of sulphur, and an ounce of spermaceti cerate, which is to be allowed to remain in contact with the morbid growth for twenty-four hours.

The *Arsenical Paste of Frère Cosme and Rousselot*, which is officinal in

France, is composed of one part of arsenious acid, two of dragon's blood, and two of porphyrized cinnabar, made into paste with mucilage when applied. There is no reason for believing that any of the almost innumerable substances which have been proposed as a basis for arsenious pastes possess any marked advantages: the only needful direction is to mix the caustic with from eight to ten times its bulk of inert material of such a nature as to make either an ointment or a paste, as the whim of the surgeon or the circumstances of the case may dictate, and to allow this to remain on for from eighteen to twenty-four hours.

ZINCI CHLORIDUM, U. S.—*Chloride of Zinc* is made by the action of muriatic acid upon zinc. It occurs in broken fragments of a grayish-white color, translucent and waxy in appearance, of an acrid corrosive, or, when diluted, acrid astringent, metallic taste. It is extremely deliquescent, fusible, volatilizable at a high temperature, and very soluble in both water and alcohol. Chloride of zinc is a very powerful caustic, producing, when applied in a concentrated form, intense pain lasting for six to eight hours, and a whitish eschar, which usually separates in from six to twelve days. Its penetrating powers are said to be a little less than those of caustic potash, and its action is certainly much less rapid and diffusive. It is a superior caustic, because its action is more readily controlled than that of potash, because its absorption does not endanger life, as is the case with arsenious acid, and because it leaves a slough which is free from odor.

Canquoin's Paste is made by mixing the chloride of zinc with flour and water. The strength varies according to the purpose, the weakest paste containing only one part of the caustic in six parts; the strongest, one part in three. When used, ten or fifteen drops of water are added to the paste, which is applied in layers, successive applications being required when a large tumor is to be destroyed. Anhydrous sulphate of calcium has been especially commended by Dr. A. Ure, as forming a drier paste with the escharotic and limiting its action more definitely to the site of application than any other substance. Concentrated alcoholic or watery solutions of the chloride of zinc are often used as caustics in cases of *chancres* and other small *specific ulcers*, and are reputed to be efficient. They should be applied by means of little pledgets of lint. As the action of the chloride upon the skin is slow and very painful, whenever the cuticle over the part to be destroyed is sound it should be removed by means of blisters. By some surgeons the escharotic is introduced directly into the tumor to be destroyed. Thus, Maisonneuve makes a paste of one part of the chloride with three of flour and a little water, then cuts these into pointed strips or "arrows" and dries them. He then thrusts these hardened bodies into the tumor,—if necessary, first making incisions with the bistoury,—in such a way that they lie close together and form a ring around the base of the tumor. A continuous slough is thus created, which cuts off the remainder of the mass from the sound tissue and causes its death. Sometimes Maisonneuve simply thrusts these arrows into the body of the tumor, and destroys it directly. The officinal *solution* (*Liquor Zinci Chloridi*, U. S.) is used as a disinfectant.

HYDRARGYRUM CHLORIDUM CORROSIVUM.—*Corrosive Sublimate* is an escharotic of moderate power, which shares the dangers of arsenic, since death has followed its external use. In saturated solution it is much used as a caustic in *chancres*, but is scarcely equal to the acid nitrate of mercury. In these cases it should be applied by means of a camel's-hair brush. Prof. George B. Wood recommends very highly in *onychia maligna* the use of a powder composed of equal parts of corrosive sublimate and sulphate of zinc intimately mixed. This powder is to be sprinkled thickly over the diseased surface, and a pledget of lint thoroughly wet with laudanum is to be laid thereon. There is severe pain for half an hour to an hour; but the dressings are not to be removed until eight or ten hours have elapsed. When the slough which is thus formed separates, a healthy granulating surface is left behind.

LIQUOR HYDRARGYRI NITRATIS, U. S.—Solution of the acid nitrate of mercury is a nearly colorless, highly corrosive, acid liquid, having a specific gravity of 2.165, and made by dissolving mercury, or its red oxide, in a large excess of nitric acid. It contains free nitric acid and the binitrate of the deutoxide of mercury. I do not know of its external use ever having produced death; but it has caused salivation, and it is perfectly conceivable that its careless employment should lead to much more serious results: indeed, in the *Lancet* for Jan. 3, 1874, is reported a very serious case of poisoning by the application of the pernitrate to a space not bigger than a half-crown. It is rarely used, except for the purpose of destroying *specific* or *cancerous ulcers*. It is especially useful in *chancres*, to which it should be applied with a glass rod. In obstinate *acne*, a minute drop applied by means of a glass brush to the top of an indolent tubercle is said to destroy it without producing a scar. It has been largely employed by gynæcologists in *ulcerations of the cervix uteri*. Its action in all these cases is very prompt and is moderately deep; the pain is severe, but transient.

ACIDUM SULPHURICUM.—*Sulphuric Acid* is a powerful escharotic, and has been used extensively for the purpose of destroying even large growths. For this purpose the strongest acid is mixed with charcoal, so as to make a thick, manageable paste. Before the application of this, the skin should be removed by a blister. At present this escharotic is not much employed.

ACIDUM NITRICUM.—*Nitric Acid* is a powerful caustic, which is never employed to destroy large growths, but is a favorite application to *chancres*, to *syphilitic*, *phagedænic*, and other unhealthy *ulcers*, as well as to *condylomata* and other small *dermal growths*. It is applied by means of a glass rod or a splinter of wood A drop or two is usually amply sufficient; and when the action has gone far enough, the part should be washed with soapsuds, which at once arrests action and causes the severe pain to cease.

ACIDUM MURIATICUM.—*Muriatic Acid* is capable of acting as a caustic, but is less powerful than either sulphuric or nitric acid, and is rarely used.

ACIDUM CHROMICUM.—*Chromic Acid* occurs in anhydrous acicular crystals, of a deep-red color, and an acid, metallic, corrosive taste. They are very deliquescent, melting down, when exposed to the air, into a deep-red solution. Chromic acid is a very active oxidizer, and when mixed with organic matter rapidly alters it, and if in slight excess will dissolve almost any form of tissue. It is no doubt in this way that it acts as an escharotic. It is very much used to destroy *condylomata* and other *dermal growths*, and no doubt would be efficient in cases of larger tumors. In superficial affections it is best applied by means of a glass rod, the liquid formed by the spontaneous deliquescence of the crystals being used. Chromic acid is sometimes prescribed dissolved in, or made into a paste with, glycerine, but it is stated that in mixing the two great care must be taken to add the liquid slowly drop by drop, as otherwise there is danger of an explosion (*Phila. Med. Times*, iv.). Care must be exercised in the free use of chromic acid,* as it is a violent poison, and has produced death when employed locally (*Stricker's Jahrbücher*, 1877, p. 139; also *Schmidt's Jahrb.*, Bd. cci. 1884, 129).

BROMUM, U. S.—*Bromine* is a dark-red liquid which has a very powerful, disagreeable, chlorine-like odor, and at ordinary temperatures emits exceedingly acrid, pungent fumes. It is sparingly soluble in water, more soluble in alcohol, and still more so in ether. Alcoholic and ethereal solutions lose their color and become acid in a few days, from the generation of hydrobromic acid. When bromine is brought into contact with organic matter, it oxidizes and completely destroys it with great rapidity. On account of its liquid form and of this property, bromine is one of the most severe, thorough, and rapid of all the caustics. It has not been much employed to destroy morbid growths, but during our late war was found to be the most efficient of all the applications tried in *hospital gangrene*. After most of the slough had been cut away, the caustic was applied pretty freely to the living tissue by means of a glass rod. The pain was very severe; but it ceased after a few moments when the caustic was washed off.

Sulphate of Zinc and *Sulphate of Copper* are feeble escharotics, never used to destroy sound tissue. *Burnt Alum* belongs in the same category, but is probably a little more feeble. All three of these drugs are used to destroy *exuberant granulations* in ulcers.

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* For experiments on its effect on animals, see *Arch. f. Exper. Path. u. Pharm.*, vi.; also *Stricker's Jahrb.*, 1877, p. 139.

CLASS XIII.—DEMULCENTS.

THESE are bland substances, which form more or less gummy or mucilaginous solutions in water, capable of exerting a calming or soothing influence upon inflamed surfaces. Without doubt water itself is the demulcent *par excellence;* but the remedies here discussed do seem to enhance its power. It has been claimed for these medicines not only that they soothe surfaces to which they are immediately applied, but also that taken internally they relieve irritation in distant organs. As, however, all of them are complex vegetable products, as many of them are staple articles in the world's food and as none of them have been detected in the blood or the secretions, it cannot be allowed that they reach distant parts through absorption into the blood. What is certainly true of some of them is probably true of all,—*i.e.*, digestion of them occurs in the primæ viæ. The relief which undoubtedly follows their use in certain affections of parts which they can reach only through the circulation is probably in great part, if not altogether, due to the large quantities of water with which they are administered, which, passing through the body, lessen the concentration, and hence the acridity, of the urine and other secretions.

Clinically, demulcents are useful as local applications in all forms of acutely-inflamed surfaces, and they are taken internally in acute *inflammatory* conditions of the *alimentary canal.* In slight *bronchial irritation* they are often of service, especially when allowed to dissolve slowly in the mouth: used in this manner, they not only exert an influence upon the mucous membrane of the mouth, but very probably find their way also into the respiratory passages.

ACACIA—GUM ARABIC. U.S.

A gummy exudation from Acacia vera and other species of Acacia, small trees growing in Northern Africa, Senegambia, Guinea, etc., the Cape of Good Hope, and Australia. Gum arabic occurs in roundish or irregular pieces, more or less transparent, hard, brittle, varying in color from white or yellowish white to red, or even deep orange brown. It consists of a peculiar principle, *Arabin*, united with about three per cent. of lime, potash, and magnesia. According to Husemann, pure *arabin* is an amorphous substance, glassy and transparent when dry, but milk-white when moist, and having a feeble acid reaction, with the power of uniting with bases. In the plant, arabin, like other gums, appears to be formed by a retrograde metamorphosis of cellulose. Indeed, Wigand declares that the flesh and even the hard endocarp of the plum can undergo this metamorphosis. The same investigator affirms that *bassorin* is a first product of the change, and is, by a continuation of the process, converted into arabin.* On account of its solubility and pleasant taste, gum arabic is often used as a demulcent in irritation of the fauces and in *angina*. It is also sometimes used as an addition to drinking-water in fevers, and is believed to have some slight nutritious properties. Its chief use, however, is in Pharmacy, in the making of emulsions, pills, etc. The *mucilage* (*Mucilago Acaciæ*) is officinal.

TRAGACANTHA, U.S.—*Tragacanth* is the concrete juice of Astragalus verus, a small shrub of Asia Minor. Tragacanth occurs in large, whitish, horny, waved flakes, or sometimes in filamentous pieces. It is odorless and nearly tasteless. Introduced into water it does not dissolve, but swells up into a soft paste. One hundred parts of it contain, according to Guérin, 53.3 parts of arabin, 33.1 parts of bassorin, and 2.5 parts of inorganic ash. Bassorin is a gummy principle, at once distinguished from arabin by its not dissolving in water, but simply swelling up into a pasty mass. Tragacanth is used in medicine only in the manufacture of troches and in suspending heavy powders, for which purpose the difficulty of its solution and the extreme viscidity of its mucilage especially fit it. Its *mucilage* (*Mucilago Tragacanthæ*) is officinal.

ULMUS, U.S.—*Slippery Elm* is the inner bark of Ulmus fulva, a large indigenous tree. The bark is of a yellowish-white or tan color, fibrous, yet when dry somewhat brittle, and occurs in long, flat strips or pieces one or two lines thick. It is pleasantly mucilaginous when chewed. It contains a large quantity of a peculiar mucilage, which it yields freely to water. Its infusion is sometimes taken in large quantities in *inflammations* of the *intestines* as a demulcent laxative; but its chief use is as an external application. When ground into powder, slippery elm makes a very excellent soothing poultice. The *mucilage* (*Mucilago Ulmi*) is officinal.

CETRARIA, U.S.—*Iceland Moss* is the fronds of a lichen, Cetraria Islandica, growing on rocks in Iceland, and in most of the northern portions of the world. It is said to be abundant in the mountains of New England. The foliaceous, dry, shining, lobed, and laciniated fronds are about four inches long, of various intermixed colors, gray, brown, and red, of a mucilaginous, bitter taste. Iceland moss contains a peculiar starch-like principle, lichen starch, and a bitter principle. It is inodorous, and has a mucilaginous, bitter taste. It yields to cold water its bitterness; to boiling water all of its virtues. *Cetrarin*, or *Cetraric Acid*, is the bitter principle, which may be obtained as a snow-white mass of interlaced acicular crystals. It unites with alkalies to form salts. With it in the lichen is associated in small quantities *lichstearic acid*. *Lichenin*, or *Lichen Starch*, the mucilaginous, nutritive principle of Iceland moss, differs from ordinary starch in not being deposited in granules within the cells, but in layers or irregular masses between the cells, or indeed forming the walls themselves of the cells (De Bary, *Hofmeister's Handb. der physiolog. Botan.*, Bd. ii. p. 255). In cold water it swells up without dissolving; in hot water it dissolves, and on cooling condenses into a jelly. With iodine it strikes a yellow, green, or sometimes rather faint blue, color. It is found in very many lichens; also in many species of sea-weed, notably in the so-called *Corsican moss*. Iceland moss has enjoyed some reputation as a demulcent in pectoral complaints. From its bitter principle it is probably somewhat tonic, and its lichenin is probably about equal to ordinary starch as a nutrient. When prepared as an article of diet, in the form of jelly, the bitter taste should be removed by soaking for some hours in a very weak cold alkaline solution, and afterwards for a little while in cold water.

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* The reader interested in the method of formation of the gums is referred to the following papers: Kützing, *Archiv d. Pharmacie*, 1851, Heft i.,—translated in the *American Journal of Pharmacy*, vol. xxv. p. 37; Mohl, *Botanische Zeitung*, 1857, p. 33; A. Wigand, *Jahrbücher für Wiss. Botanik*, 1861, iii. 117; and for a general discussion by Dr. J Sachs, to *Hofmeister's Handbuch der physiologischen Botanik*, Bd. iv. p. 367.

CHONDRUS, U.S.—*Irish Moss, or Carrageen.*—The fronds of Chondrus crispus, a sea-weed growing on the coast of Ireland, and also on the northern coast of the United States, where it is now gathered in large quantities. The fronds are purplish red,—but, as kept in the shops, bleached by washing in fresh water, whitish, and translucent,—cartilaginous, slender, much branched, swelling up but not dissolving in water, and having a slightly saline taste Their virtue depends chiefly upon a starch- or gum-like principle, *Carrageenin*, which is distinguished from starch by not turning blue with iodine, from gum by not precipitating from its watery solution on the addition of alcohol. Chondrus also contains a notable proportion of a vegetable albumen, very rich in nitrogen.

Carrageen, being demulcent and nutritious, is employed as an article of diet in those cases requiring food of such character, and may be used instead of arrow-root. It is to be prepared by first soaking for ten minutes in cold water, and then boiling from half an ounce to an ounce of it (according to the desired consistency) in a pint and a half of water down to a pint, sweetening and flavoring to taste. Milk may be substituted for water, and the preparation thus rendered more nutritious.

GLYCYRRHIZA, U.S.—*Liquorice Root* is the root of Glycyrrhiza glabra, a native herb of Southern Europe. It occurs in long cylindrical pieces, from a few lines to more than an inch in diameter, brownish externally, and yellowish within. Its fracture is fibrous, its taste sweet and mucilaginous, its odor none. Its active principle is *Glycyrrhizin*. This is a sweet, neutral substance, differing from the sugars in not being converted by nitric acid into oxalic acid, and by its inability to undergo the vinous fermentation. Liquorice root is very largely used as a demulcent in pectoral complaints, and, on account of its pleasant taste, as a means of disguising or of flavoring medicines. In the form of glycyrrhizin it is said to conceal almost entirely the bitter taste of quinine and similar substances. It is used almost exclusively in the form of the *extract* (*Extractum Glycyrrhizæ*, U.S.), known as *Liquorice*. The *Mistura Glycyrrhizæ Composita*, U.S., or *Brown Mixture*, contains paregoric, antimonial wine, and sweet spirit of nitre, and is much used as a domestic remedy in "*colds*" and the early stages of *mild bronchitis*. The dose for an adult is half a fluidounce to a fluidounce every three hours; for a child three years old, a teaspoonful. The *pure extract* (*Extractum Glycyrrhizæ Purum*, U. S.) and the *fluid extract* (*Extractum Glycyrrhizæ Fluidum*, U. S.) are excellent preparations. *Glycyrrhizinum Ammoniatum*, U. S., is a very elegant preparation, which, however, is incompatible with acid or alkaline solutions; its dose is from five to ten grains.

MEDULLA SASSAFRAS, U. S., is the pith of the indigenous sassafras, which yields a delicate mucilage with water. This mucilage, which is much used in diseases of the eye, is officinal (*Mucilago Sassafras*).

ALTHÆA, U. S.—The roots of the Althæa officinalis yield a bland mucilage, and are occasionally employed to make a decoction, which is given in irritated states of the stomach and bowels, or in the form of a syrup as a vehicle (*Syrupus Althææ*, U. S.).

LINUM, U. S., or *Flaxseed*, is the seed of Linum usitatissimum, or common flax, and contains large quantities of mucilage and of oil: its *Compound Infusion* is much used internally. It is often made with boiling water; but the application of too much heat causes the extraction of more or less of the oil, and thereby renders the preparation less palatable. The infusion should never, therefore, be boiled during its making. The addition of lemon and sugar renders it more palatable. It may be drunk *ad libitum* in pectoral *catarrhs*, in *enteritis* and *dysentery*, and in *irritation* of the *kidneys* or the *urinary passages*. *Ground flaxseed* (*Lini Farina*) is especially adapted, by the oil and mucilage it contains, for making poultices.

The seeds of the *quince* (*Cydonium*, U. S.) contain a large quantity of mucilage, which they readily yield to water, forming a thick tenacious solution (*Mucilago Cydonii*, U. S.).

TAPIOCA is the fecula of the root of Janipha Manihot, a native of South America. There are two varieties of the tapioca plant, the *sweet* and the *bitter cassava*. The latter is in its fresh state poisonous, from the prussic acid which it contains, but yields most, if not all, of the tapioca of commerce. The tapioca is obtained by allowing the expressed juice to stand, separating the powder which deposits, washing, and drying by heat, owing to the action of which the starch is rendered partially soluble in cold water. It is in irregular, hard and rough, nearly tasteless grains, which the microscope shows to be composed of broken, ruptured starch-granules. It constitutes an elegant farinaceous article of diet, and may be prepared in the following manner: Soak two tablespoonfuls of very clean tapioca in two teacupfuls of cold water over-night; in the morning add a little salt and one pint of milk, or water if milk is not allowed; simmer it until quite soft; stir well while cooling; when done, pour into a bowl, and add sugar, wine, and nutmeg, according to taste or the exigencies of the case.

MARANTA (*Arrowroot*) is a fecula or starch, obtained from the rhizome of the Maranta arundinacea, a native of the West Indies. Arrowroot is produced in the West Indies, in Africa, and in the Southern United States, especially Florida. The most esteemed variety is that which comes from the island of Bermuda. It is obtained in the usual method by beating the root-stocks into a pulp, and the use of flowing cold water. It occurs as a very light, tasteless, and odorless white powder, which the microscope shows to be composed of ovate, oblong, or irregularly-convex granules, from the seven-hundred-and-fiftieth to the two-thousandth of an inch long, marked with very fine rings and a circular hilum, which cracks in a linear or stellate manner. It is often adulterated with other starches, which are best detected by the microscope.

Arrowroot affords the most readily prepared and, in the sick-room, the most popular of all the farinaceous articles of diet. It may be prepared in the following manner: Stir two teaspoonfuls of arrowroot in half a teacupful of cold milk until a *perfectly smooth* mixture is made; have on the fire a pint of milk, and, while this is boiling, add the arrowroot little by little, stirring constantly until cooked,—*i.e.*, from one to two minutes after the last is poured in; add sugar, nutmeg, and wine, according to taste or the exigencies of the case. When milk is not to be had, or a very low diet is required, water may be substituted.

SAGO is a fecula obtained from the pith of Sagus Rumphii and other sago palms of Sumatra and the neighboring regions. It is first prepared in the usual manner, and then formed into a paste with water, rubbed into grains, and dried. *Pearl Sago* occurs in hard, roundish, somewhat translucent or sometimes opaque grains, about the size of a pin's head. *Common Sago* is in larger and browner grains, often mixed with some powder. It is composed of oval or ovate, often truncate and muller-shaped, often much broken, starch-granules. It is used exclusively as an article of diet, forming a jelly, which is best prepared as follows: Wash the sago well in cold water; put a small teacupful of it to soak in half a pint of water over-night, and in the morning put this mixture into one pint of hot water; squeeze into it the juice out of a thinly-pared lemon, and allow to simmer slowly for twenty minutes; then sweeten, add wine according to taste or the exigencies of the case, then pour into moulds to cool.

CANNA, or *Tous les Mois*, is a starch which is prepared in the West Indies, and resembles potato starch, but has a remarkable satin-like lustre, due to the extraordinary size of its granules. It forms with water a tenacious jelly, which is not so clear as that produced by arrowroot. It is very rarely, if ever, used in this country.

HORDEUM.—Under the name of *Hordeum*, or *Barley*, the United States Pharmacopœia recognizes the decorticated seeds of the common barley, the pearl barley of commerce. They contain starch and mucilage, and the *decoction* (*Decoctum Hordei*) was formerly officinal. *Barley-water* is used as a nutritious, demulcent drink in fevers and inflammatory conditions, especially when the gastric mucous membrane is involved. The U. S. Pharmacopœia 1870 directed that it should be prepared as follows: "Take of barley two troyounces; water a sufficient quantity. Having washed away the extraneous matters which adhere to the barley, boil it with half a pint of water for a short time, and throw away the resulting liquid. Then, having poured on it four pints of boiling water, boil down to two pints, and strain."

CLASS XIV.—EMOLLIENTS.

TRUE emollients are perfectly bland, fatty substances which, when applied to the skin, soften it and render it more pliable. The action of these remedies is largely mechanical, and they probably soften the derm in precisely the same way as they affect a raw hide or a piece of leather. They are therefore especially useful when the skin has a tendency to crack or to chap. Whenever surfaces become sore by attrition, or, in other words, chafe, emollients are also useful in a mechanical method. Emollients often afford relief in simple inflammations of the skin under such circumstances that their action cannot be explained in any of the ways alluded to: indeed, they seem to exert a dynamic influence upon the nutrition of the parts concerned. To the best of our present knowledge, the oxygen or other constituent of the air acts as a stimulant to exposed surfaces and increases inflammations there present; and it is believed that fatty matters do good by keeping out the air. If this be so, the apparently dynamic influence of fatty matters is, after all, mechanical. Be these things as they may, clinical experience has demonstrated that fatty matters are of very great value in the treatment of superficial inflammations. It must be borne in mind that the blandest fat, when it becomes rancid, is very irritating, and will do far more harm than good. In the use of fatty emollients, the strictest attention must therefore be paid to the condition of the material employed. Any perfectly bland oily substance may be used as an emollient. *Mutton suet* and *goose-grease* are famous in domestic medicine, but are simply valuable because, if well prepared, they are less apt than some other fats to become rancid. It cannot be allowed that there is any difference in fats, unless it be in penetrating power: a very hard fat is of course not so readily applied as a softer one, and therefore only such fats as freely melt, or at least become very soft, at the temperature of the body, are to be used. *Common Lard* (*Adeps*, U. S.), when freed by washing from the salt which it commonly contains, is a mild fat, melting at the temperature of the body. It is enormously used in pharmacy. *Cacao Butter* (*Oleum Theobromæ*, U. S.) is an absolutely bland vegetable fat, which is a firm solid at ordinary temperatures, but melts with the heat of the body, and is consequently very largely used in the preparation of suppositories, both officinal and magistral. *Spermaceti* (*Cetaceum*, U. S.) is also employed to give consistence to ointments, as is also wax (*Cera alba*, or *white* *wax*, and *Cera flava*, or *yellow wax*, U. S.). *Cold Cream* (*Unguentum Aquæ Rosæ*, U. S.), containing oil of sweet almonds, spermaceti, white wax, and rose-water, is the most elegant of all the officinal fatty emollients, unless it be glycerine, which is so much used that it merits a distinct notice.

GLYCERINUM—GLYCERINE. U.S.

This is a thick syrupy liquid, colorless, and free from odor, but of a sweet taste. It was originally prepared by heating together a metallic oxide and ordinary fats, as in the manufacture of lead-plaster. Chemically speaking, it belongs to the alcohols, and is known, according to the recent nomenclature, as *propenyl alcohol*. It is always set free during the process of saponification, when the stearic or other acids of the fat unite with some base to form salts, known as soap. Consequently, glycerine always forms a considerable part of the soap-maker's waste; but in this it is so mixed with impurities that until recently it was valueless. Now, by means of certain patent processes, the glycerine is said to be obtained pure from the waste products of soap-factories. It is also manufactured on a very large scale by the direct decomposition of fats by heated steam, in accordance with a plan patented by Mr. Tilghman. The great bulk of the glycerine in commerce is at present prepared in this way.

Under certain circumstances, not well understood, glycerine forms hard, brilliant crystals. In its usual liquid form it mixes in all proportions with water and alcohol, and possesses itself very great solvent powers, dissolving iodine, bromine, the alkalies, tannic and other vegetable acids, a large number of neutral salts, salicin, and very many other organic principles, so that it is largely used in pharmacy.

Glycerine does not evaporate upon exposure, but is very hygroscopic, and absorbs water from the air. When pure, it is incapable of becoming rancid or of fermenting spontaneously. The acrid glycerine, formerly so abundant in commerce, and still met with, owes its irritant properties to contaminating substances, especially, it is said, to oxalic and formic acids. The former of these substances is apt to be created by the action of the sulphuric acid used during the purification of the glycerine, the latter by the reaction between the oxalic acid and the glycerine.

PHYSIOLOGICAL ACTION.—When large doses of glycerine (in the dog eight or more parts per thousand by weight) are injected subcutaneously, death is produced in a period varying, according to the dose, from one hour to several days. The symptoms are loss of muscular strength, lethargy, bloody urine, vomiting, dryness of the mucous membrane with marked thirst, fall of temperature, gradual extinction of both respiration and circulation, and finally convulsions and coma (Dujardin-Beaumetz and Audijé, *Bull. Thérap.*, xci., p. 62). The convulsions occur more early and severely when large doses are employed, and are then said to be tetanic, and to be accompanied with a decided rise of temperature. The fall of temperature is, even in the milder cases, only present late in the poisoning, and is sometimes, if not always, preceded by a rise. After death intense congestion, with more or less softening of the tissue, is found in the lungs, kidneys, and intestines. In man no symptoms of poisoning have ever been produced by glycerine; the largest single amounts ingested—an ounce or so—having no perceptible effect other than that of a laxative.

Catillon claims that glycerine administered in small continuous doses exerts a decided effect upon nutrition (*Bull. Thérap.*, xcii., p. 130; *Archiv. Physiol. Norm. Path.*, 1877). In his experiments he found that eight grains given daily to guinea-pigs produces a very marked gain in weight, with a lessened excretion of urea. In man an ounce daily also produced, in the elimination of urea, a decided diminution, which was not increased by increasing the doses of glycerine. The appetite in many cases was, after a little time, much improved, and then the increased ingestion of food produced an increased elimination of urea. The fact that an increase of food was permitted in these experiments shows, however, that the conditions of experimentation were not sufficiently rigid to allow much weight to be attached to the result; and the relation of glycerine to the elimination of urea has been recently investigated by L. Lewin (*Zeitschr. f. Biologie*, xv.), by N. Tschirwinsky (*Ibid.*), and by Dr. I. Munk (*Virchow's Archiv*, lxxvi. 130), with somewhat contradictory results. Of these experiments the most extensive are those of Munk, who seems to have used all proper precautions, and found that glycerine has no effect upon the elimination of urea or the general bodily nutrition. The results reached by Lewin correspond with those of Munk. Tschirwinsky omitted fatty materials from the food, and found that whilst at first the elimination of urea was diminished, it afterwards, under the use of very large doses of glycerine, was increased.

With our present evidence it must be considered most probable that glycerine has no controlling power over the waste of nitrogenous tissues, but there is reason to believe that it is in some manner burnt up in the system, and has, therefore, some slight food value. It is undoubtedly absorbed, and when given very largely can be recognized in the urine, which, in some experiments, Tschirwinsky found to contain as much as 8.7 per cent. of it. Even when given freely it seems to be, at least in part, changed, since both Ustimowitsch (*Arch. f. d. Ges. Physiolog.*, xiii. 453) and Plósz (*Ibid.*, xvi. 153) have found a new substance in the urine which they believe to be a derivative product from glycerine. M. Catillon found that it was not eliminated by the skin or intestines even when it purged, and was only partially eliminated with the urine, whilst, in a series of very careful experiments, Munk found that when given in small quantities it cannot be detected in the urine. According to Fuchsinger, the bloody urine produced by poisonous doses contains an abundance of the coloring matter of the blood, but no free corpuscles (*Pflüger's Arch.*, Bd. xi. p. 502). Very interesting in connection with the use of glycerine in diabetes is the assertion of Fuchsinger

(*Pflüger's Archiv*, xii., p. 501; *Centralb. Med. Wiss.*, 1877), that in rabbits slightly poisoned with glycerine no sugar appears in the urine after the "diabetic puncture." The experiments of Eckhard gave, however, a contrary result (*Centralb. Med. Wissen.*, 1876, p. 273), and Catillon affirms that given in very large continuous doses glycerine increases the amount of sugar in the blood.

THERAPEUTICS.—Locally applied, glycerine is perfectly unirritating, and is much employed as an emollient. The chief disadvantage that attends its use is its stickiness; on the other hand, its non-volatility and its hygroscopic properties give a persistency to its action which is often very advantageous. It enters largely into the composition of popular emollient ointments, or "creams," as they are called, and is often used itself for chapped hands, excoriations, and similar troubles. It is also employed by dermatologists to some extent in *chronic eczema;* in *seborrhœa*, whether affecting the hairy scalp or other parts, it is asserted to be especially useful, softening the masses of secretion, and, used in conjunction with such remedies as borax, zinc, and acetate of lead, diminishing the amount of secretion. When there is a want of sebaceous secretion, it is said also to act efficiently; in *scabies*, *pruritus*, and even *psoriasis*, glycerine is used, diluted with water, as a vehicle for more active remedies. Upon the mucous membranes glycerine acts very much as it does upon the skin, and diluted with water is very useful in *coryza*, and even, by enemata, in *dysentery;* in *croup* or *laryngitis* it may with advantage be applied freely by means of a large camel's-hair brush to the orifice of the larynx, so as to run into the latter. In laxative doses it is asserted to be very effective in *hemorrhoids*. It also forms an excellent basis for mouth-washes; or a paste may be made with it and borax, or similar substance, for use in ulcerations of the same cavity. The list of diseases in which this remedy is employed might be very much lengthened; but the examples already given are sufficient to indicate the range of its application as an emollient and a vehicle. There are certain persons upon whose skin and mucous membranes even the purest glycerine seems to act as an irritant. This influence is most intense when the glycerine is nearly or entirely free from water. It is, however, discernible even when the remedy is much diluted, and often prohibits its use. The existence of this idiosyncrasy to glycerine can be determined only by trial.

When administered internally in doses of one or two ounces, glycerine acts as a gentle but very uncertain laxative. I do not think that a single dose has any other perceptible effect. It was long ago proposed as a substitute for cod-liver oil in *cachectic diseases*, but failed to acquire reputation. Nevertheless, the results of Catillon would seem to demand for it more extensive trial. That observer states the proper amount of it to be half an ounce to an ounce in the course of the day in three doses. It has also been proposed and highly commended in *diabetes*.* It appears to be harmless in this affection, and therefore may be used as a sweetening-material for coffee, tea, and other beverages; but there is no reason to believe that it exerts any control over the disease. The most important internal use of glycerine is as a harmless substance which has the power of disguising nauseous medicines. In this way it may be employed with castor oil, in emulsions of turpentine, in solutions of iron, and in various mixtures. It seems, as it were, to envelop the medicinal substances and prevent their acting on the palate. *Plasma*, or *Glycerite of Starch* (*Glyceritum Amyli*, U. S.), is often used as a protective: *Glycerite of Yolk of Egg* (*Glyceritum Vitelli*, U. S.) is chiefly employed in making emulsions.

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* For literature and discussion of point, see *Ziemssen's Encyclopædia*, vol. xvi.

POULTICES.—Under the head of Emollients I shall also speak of poultices, which are moist, soft, scarcely adhesive, perfectly bland plasters, used to a very great extent to combat superficial inflammation. Poultices are much more powerful agents than the true fatty emollients, and are much more capable of being abused: the results of such abuse will be spoken of directly. A poultice may, of course, be stimulating and irritant if made of such a substance as mustard; but the emollient or true poultice is prepared out of some bland material, which is totally free from action upon the skin. I do not think that there is any difference whatever in the action of the various substances usually employed in the preparation of poultices, the latter depending for their remedial powers solely upon the warmth and water which they contain. Water, when pure and of a temperature approximating that of the body, is a sedative, checking all action, possibly by a direct influence, but probably by the merely mechanical acts of dilution of the pabulum and of separation of the germinal granules. It is also a relaxant, rendering all tissues soaked in it soft and yielding.

Poultices are sometimes applied in the early stages of phlegmonous and other superficial inflammations, for the purpose of checking the morbid action. Their influence is in such case simply one of sedation, and they are certainly not so efficient as the cold-water dressing. They are, however, especially useful in the advanced stages of inflammation, when suppuration has already commenced or is about to set in. Clinical experience has demonstrated that they now favor the formation of pus. It is hardly worth while to discuss how they do this, so long as the natural method in which pus is produced is a matter of dispute. If, as Cohnheim believes, pus is composed solely or largely of out-wandering white blood-corpuscles, it is evident that the relaxing influence of a warm poultice will greatly facilitate the escape of these bodies. Further, the poultice in the latter stages of a superficial phlegmon not only hastens the formation of pus in the inflammatory focus, but lessens irritation in the outlying parts by its sedative action, and so softens the tissues as to aid in the passage outwards and the discharge of the inflammatory products. When poulticing is too long persisted in, the part becomes pale or white, swollen, relaxed, and has a sodden look; the granulations of the ulcer or abscess are large, pale, and very flabby, and all the vital actions are below the normal point. It is possible that even death of a part might be brought about by continuous poulticing. Be this as it may, after the discharge of pus, whenever the parts put on the aspect just spoken of, the poultice should be removed and stimulating applications be substituted.

So far, the use of poultices to combat external inflammations has alone been spoken of; but clinical experience has demonstrated their value in internal inflammations, even when such deep-seated tissues as the lungs are affected. Their action in these cases is somewhat different from that which they exercise over superficial inflammations. According to the dictates of experience, they should be applied very hot, and be frequently renewed; very often, too, a small amount of mustard or of some similar stimulating material is added to them with advantage. As a result, these poultices act as gentle but deep-reaching counter-irritants, which in all likelihood affect not merely the blood-vessels of the skin, but also those of the subdermal tissue. When it is borne in mind that in all these cases the poultice is applied to a very large surface, it will be readily perceived that this counter-irritation is a powerful one. Thus, in *pleurisy*, or in *pneumonia*, the whole anterior or posterior surface of the chest is covered, or perhaps the whole chest is enveloped, by the jacket-poultice. In *peritonitis*, the poultice should be as large as the abdomen of the patient. Now, in either of the cases mentioned, it is plain that the amount of blood drawn to the surface must be considerable. I cannot help surmising that the water of the poultice in some cases actually soaks through and reaches the affected tissue so as to exert its direct sedative influence upon it. In lung-diseases of children, whose chest-walls are very thin, the value of poultices has seemed to me much greater than in corresponding affections in adults; and it is not illogical to believe that the difference may be dependent upon the inequality of the chest-walls.

Flaxseed meal is the most frequently-used substance for making poultices, for which purpose the large amounts of oil and mucilage which it contains especially fit it. Ground *slippery elm* makes a very elegant demulcent, mucilaginous poultice. Ordinary mush from *Indian meal* affords a cheap and very serviceable material, and *bread and milk* makes a popular, very mild and unirritating, but expensive poultice. When a poultice is to be applied to affect internal organs, and consequently has to be large and capable of holding the heat for a long time, the choice of material lies exclusively between flaxseed and Indian meal. The former of these is the more adhesive, and makes the more manageable poultice; but popular belief, and I think with reason, attributes to mush a superior power of retaining heat. In either case the poultice should be put on as hot as it can be borne, and should be covered by a large piece of silk oil-cloth, which aids in retaining not only the moisture, but also the heat. The interval of renewal should be short, and should be governed solely by the rapidity with which the applied poultice grows cold.

CLASS XV.—DILUENTS.

A DILUENT is an indifferent substance which is absorbed and in its passage through the body simply dilutes the various fluids of the organism as well as the excretions. The only diluent is water, which is given in various forms. Thus, the natural medicinal waters owe much of their value to the large quantity of water they contain. It is evident that when a quart of water more than usual is taken into the system, it must whilst it stays there lessen the concentration of the bodily liquids, and must finally in some way find an exit from the body. The increased excretion even of water means increased action in the eliminating glands; and the water passing out of the blood must always carry with it more or less of the soluble matters contained in the same, so that whilst the percentage of solid matter in the urine or in the sweat may be lessened by large potations of water, the actual amount eliminated is no doubt increased. Hence water acts not only as a diluent, but also as a depurant.

It is especially in regard to the urinary organs that water is employed medicinally, with three distinct possible objects. Thus, it may be used simply to aid the re-establishment of completely or partially suppressed renal secretion. During a recent visit to Bellevue Hospital, New York, I was informed that in *acute Bright's disease* water had been found to be a most efficient diuretic, increasing very remarkably the urinary excretion, relieving the irritation of the kidneys, and aiding the return to health. In these cases at least half a pint of water should be taken every two hours. I have tried it in chronic Bright's disease, and found it to work well in some cases; but in others, no increase of the urine taking place, the water accumulated in the system and added to the distress. Again, the dilution of the urine is often important, as in *gonorrhœa*, or when there is a tendency to the formation of either *gravel* or *calculi*. Water is also used as a depurant in chronic disorders in which there is no organic disease, but an habitual torpor of the emunctories,—cases in which the liver is said to be torpid, and in which there is a foul tongue, habitual costiveness, and a scanty urine with a tendency to the formation of a lateritious deposit.* In these cases a couple of tumblerfuls of water upon rising will often produce a stool after breakfast, as well as increase the flow of urine. Very generally a mild saline may be advantageously added in small quantity to the water; and such natural mineral waters as those of Saratoga are especially beneficial.

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* For experimental evidence that water in rabbits does increase flow of bile, see Zawilski, *Centralb. für Chir.*, 1877, p. 327.

CLASS XVI.—PROTECTIVES.

In the present class are included those materials used by the physician as external applications to exclude the air and to protect inflamed dermal or other tissues. Sufficient has already been said in regard to the importance of the exclusion of the air, under the heading of Emollients. It is evident that the latter class of remedies, as well as demulcents, act as protectives; but the class of Protectives proper seems necessary for the consideration of certain remedies which act more plainly in a mechanical method and which will defend the skin against external agencies.

First to be considered under the present class are certain plasters, used to protect the skin and raw surfaces from external influences. The *adhesive plaster* (*Emplastrum Resinæ*, U. S.) is used enormously for mechanical purposes. It does, however, irritate the skin somewhat, and consequently is rarely employed where protection is the only object. Under the latter circumstances, the *lead plaster* (*Emplastrum Plumbi*, U. S.) or the *soap plaster* (*Emplastrum Saponis*, U. S.) is preferable. These substances are free from irritant properties, but are very slightly adhesive, and are scarcely used except to protect the skin from pressure or friction, as when *bed-sores* are threatened. They should be spread upon very soft kid. It is also very important that they be not so thick or hard as to lose their pliability. If they are stiff, by their movements during the motions of the body they often do more harm than good.

COLLODIUM—COLLODION. U.S.

When any finely-divided ligneous body, like raw cotton, is steeped for a few minutes in a mixture of nitric acid of the specific gravity of 1.5 and concentrated sulphuric acid, and then squeezed, thoroughly washed, and dried, it gains about seventy per cent. in weight, and is converted into a substance known as *pyroxylin*, or *gun-cotton*. The change consists in the substitution of nitryl (NO_2) for a portion of the hydrogen. There are a number of varieties of gun-cotton. The true explosive gun-cotton, that which is alone adapted for gunnery, is *trinitrocellulose*. It is not so soluble as the less highly nitrated variety, and is not fit for use in medicine. The officinal pyroxylin (*Pyroxylinum*, U. S.) is one of the more soluble varieties of gun-cotton but is not soluble to any extent in ether.

Gun-cotton is a perfectly inert substance, so far as the external surface of the skin is concerned, and probably has no effect upon the system when taken internally. It is not at all soluble in water, and its only use in medicine is in the manufacture of collodion. This substance is officinally prepared by dissolving two hundred grains of pyroxylin in a mixture of twelve and a half fluidounces of stronger ether and three and a half fluidounces of stronger alcohol. It is a colorless, slightly opalescent liquid, of a syrupy consistence, and smelling strongly of ether. By long standing it deposits a layer of fibrous matter, and becomes more transparent. This layer should be reincorporated, by agitation, before the collodion is used. When it is applied to the skin, and the menstrua are allowed to evaporate, collodion forms a colorless, transparent, flexible, and strongly contractile film, which adheres very closely, and cannot be readily removed by washing, motion of the part, or external mechanical force. As this coating is perfectly impervious to air and water, collodion is much used in surgery for various purposes. It is evident that care should be used in its application to abscesses and discharging wounds, lest it should prevent the discharge of pus. Small fresh wounds are often very advantageously dressed in the following manner, especially cuts on the fingers and about the head. If necessary, the hair should first be shaved off the part, and then a piece of coarse gauze or mosquito-netting, of suitable size and shape, should be laid so as to cover the wound and extend across each side from half an inch to an inch and a half, according to circumstances. One end should then be tightly fastened to the skin by repeated applications of the collodion with a camel's-hair brush. When the adhesion has become sufficiently firm, the gauze should be drawn so as to close the wound tightly, and whilst it is held in position the collodion should be applied all over it. As the collodion contracts during drying, the wound is more and more tightly closed, until at last a firm, perfectly tight dressing binds it close together. Of course in deep wounds this method of closure is not to be used.

The contraction of the collodion film is a great drawback to its use for certain purposes. This can be in great measure obviated and the film made more pliable by the addition of from eight to ten drops of castor oil to the ounce of the liquid. Under the name of *Flexible Collodion* (*Collodium Flexile*), the U. S. Pharmacopœia directs a preparation very similar to that just spoken of. It contains twenty grains of Canada turpentine, besides ten grains of castor oil, to the ounce; and probably the stimulant effect of the terebinthinate will make itself apparent upon some susceptible skins. Whenever collodion is used simply as a protective, one of these modified preparations is much preferable to the pure article.

Any principle which is soluble in a mixture of ether and alcohol may be added to collodion, and in this way medicinal substances may be applied to the external surfaces. The films formed are often less firm and adhesive than those of the simple collodion.

GUTTA-PERCHA, U. S., is a whitish or pinkish solid, the concrete juice of the Isonandra gutta, a large tree growing in the Malayan Archipelago. When pure it is a carbo-hydrogen, but as it occurs in the shops it contains a minute proportion of resin, vegetable, and casein. Under the influence of a mild heat it softens, and on cooling hardens again. Hence, rolled into sheets, it is much used in surgery for making splints, the piece being plunged into hot water, fitted to the limb, and allowed to stiffen.

Solution of Gutta-Percha (*Liquor Gutta-Perchæ*, U. S.) is made by dissolving small pieces of gutta-percha in purified chloroform. When it is applied to the skin, a thin elastic adhesive film is left, which protects the parts from the air. This is said to be a very elegant preparation for use in *small cuts*, *abrasions*, *chapped lips*, and the little injuries which come within the province of domestic medicine rather than that of the professional art.

DIVISION II.—NON-SYSTEMIC REMEDIES.

THESE are drugs which act not directly upon the human system or upon any of its tissues, but upon some extraneous material or entity, either in the cavities of the body or upon its exterior. Thus, an antacid neutralizes acid in the stomach, or an anthelmintic kills the tapeworm in the intestines, or a disinfectant destroys poisonous emanations in the exterior world and thereby wards off disease.

CLASS I.—ANTACIDS.

ANTACIDS are, strictly speaking, substances which are capable of neutralizing acid. The class, as here defined, contains those remedies which in medicine are used for the purpose of neutralizing an excess of acidity in the primæ viæ. They are almost solely employed in forms of *dyspepsia*. Without doubt, *cardialgia*, *gastric uneasiness*, "*heartburn*," and the rising of sour water in the mouth, are often the result of too much acid in the stomach, perhaps secreted by a perverted glandular action, but more probably in the great majority of cases formed by fermentative changes in the partially-digested food. As excessive acidity of the stomach causes gastric uneasiness and derangement, so will a similar condition of the intestinal canal cause pain and spasm and functional disturbance in the bowels. This is seen most frequently in infants, and is very often associated with a diarrhœa in which the passages have a green color, similar to that of spinach, and hence are sometimes spoken of as "spinach-stools." In *diarrhœa* of this character, as well as in *colic*, antacids are often of service by neutralizing the acid in the intestinal canal.

Clinical experience has demonstrated that dyspepsia is often permanently relieved by the use of alkalies when they are given steadily day after day, about twenty minutes after eating, for a long time. According to Dr. Thomas K. Chambers (*The Indigestions*, Am. ed., 1870, p. 67), this is dependent upon an effect pointed out by Claude Bernard, the augmentation of the acid gastric juice, and so of the normal peptic powers of the stomach. The same authority further says, "The test of benefit being derived from an alkali is the dose not requiring to be increased as the patient goes on taking it, but, on the contrary, being diminished gradually, while relief from the recurrence of heartburn continues still to be experienced."

Sick headache is sometimes dependent upon gastric irritation produced by an excess of acid in the stomach. This true sick headache is generally to be distinguished from migraine by the early occurrence of the stomach-symptoms, either as heartburn, nausea, vomiting, or simple gastric distress, and by the fact that the pain comes on with an attack of blindness or of dizziness, and is not limited to any one spot, as the supraorbital or other neuralgic foci, but is felt all across the brows. In this form of cephalalgia, antacids often afford very great relief.

Various substances which have already been discussed in this work are excellent antacids, most of them uniting this to other medicinal properties. Thus, when a stimulating antacid is desired, as is very often the case in sick headache, half a drachm of the *aromatic spirit of hartshorn* may be taken, well diluted with water. Again, when a laxative antacid is desired, a teaspoonful to a tablespoonful of *magnesia* may be exhibited. *Potassa* and its carbonates have already been dwelt upon with sufficient detail. They may be used as antacids; but, as they exert other powerful influences upon the system, they are, I think, not so generally useful as the soda preparations. Nevertheless, the *Solution of Potassa* (*Liquor Potassæ*, U. S.) is largely employed as an antacid. It is a colorless water-like liquid, of a strong, acrid, alkaline taste, and is made by boiling a solution of the bicarbonate of potassium with lime. It contains only five and eight-tenths per cent. of the alkali, but acts upon animal and vegetable substances, and imparts a distinct soapy feel to the fingers when they are moistened with it and rubbed upon one another. It is capable, in overdose, of acting as an irritant poison. The dose is ten to twenty minims, well diluted.

SODIUM.

Unlike potassium, sodium and its salts have very little influence upon the higher animals. Frogs are much more affected, it causing spinal convulsions, and slowing, or even diastolic arrest, of the heart (Podocaepow, *Virch. Arch.*, Bd. xxxiii. 507; Schönlein, *Arch. f. d. Ges. Physiol.*, xviii. 26). M. Laffout affirms that soda primarily stimulates the frog's heart (*Compt.-Rend. Soc. Biolog.*, 1880, 282). Prof. S. Ringer and Dr. H. Sainsbury find that the sodium salts are capable of arresting the cut-out frog's heart in diastole, the arrest being preceded by very little disturbance of rhythm; the amounts required were, however, so large that sodium salts can hardly be made to kill (*London Lancet*, 1882, ii., p. 736).

On the other hand, Grandeau (Robin's *Journal de l'Anatomie*, 1864) found that one hundred and seven grains of the carbonate of sodium injected into the vein of a dog produced only very slight symptoms, and that thirty-five grains of the nitrate similarly administered to a rabbit caused only some convulsive movements. According to Guttmann (*Virchow's Archiv*, Bd. xxxv.), however, the soda salts thrown directly into the blood in very large amounts will slowly cause death, the agony being very prolonged, and, when the chloride is used, convulsions being developed.

Both Podocaepow and Guttmann assert that even the largest doses do not sensibly affect the heart or the temperature; and the latter observer further declares that they are without influence upon the nerve-centres, the peripheral nerves, or the muscles.

If this be the case, however, it is difficult to perceive how they can cause death; and the earlier experiments of Podocaepow indicate that they do exert a very feeble action upon the peripheral nerves or the muscles.

Upon the blood the immediate influence of the soda salts is very slight, for Podocaepow asserts that one part dissolved in twelve parts of blood does not affect either the physical characters of the red corpuscles or the intensity of the ozone reaction.

The effect of the continuous exhibition for a few days of large amounts of salt upon the human organism has been elaborately investigated by Dr. Münch (*Archiv Vereins Gemeinschaft. Arbeiten*, Bd. vi. p. 369, 1863), and found to be very feeble. At first there was a slight diminution of excretion, and a corresponding gain of the body in weight; but after a time the excretions increased, and the weight of the body decreased. The variations in excretion affected chiefly the urine, but sometimes the perspiration and fæces were also influenced. The urine was rendered alkaline, but its solid ingredients were scarcely at all affected.

Although a certain amount of the soda salts is a necessary food for the higher animals, yet it is very doubtful whether an habitual excess of them has any decided effect upon nutrition. MM. Damourette and Hyades claim that the elimination of urea and uric acid (*Journ. de Thérap.*, 1880, 440) is markedly increased; but an examination of their experiments will show that this conclusion is not warranted by them, and in a series of experiments with the phosphate, acetate, and sulphate of sodium, Dr. I. Mayer (*Zeitsch. f. Klin. Med.*, 1881, 82–95) found no increase, and the experiments of A. Ott on the dog gave the same results (*Hoffmann u. Schwalbe's Jahresbericht*, 1883, 220). Plouriez (*Compt.-Rend.*, t. xxv.) believes that the chloride has a tonic influence: he analyzed his blood after he had used daily one hundred and fifty grains of salt beyond the ordinary amount for three months, and again after he had taken only the usual quantity. The red corpuscles were very decidedly more numerous, the fibrin slightly more abundant. and the albumen decidedly less abundant, at the first analysis than at the second.

As Bidder and Schmidt (*Canstatt's Jahresbericht*, 1852) assert that the hydrochloric acid of the gastric juice is derived from the chloride of sodium, and as Rabuteau (*L'Union Méd.*, t. xii. p. 186, 1871) found that, in dogs with gastric fistula, both the quantity and the acidity of the gastric juice are decidedly increased by the use of salt meat, it would appear probable that common salt acts as a tonic by increasing the digestive power. On the other hand, it is well known that physiologists are still disputing as to whether free hydrochloric acid exists at all in the gastric juice.* Further, it is certain that pepper or any similar condiment will, by its local action, increase the flow of gastric juice; and in Rabuteau's experiments the mere local irritation of the salt, or the difficult digestion of the preserved meat, may have given rise to the increased secretion by the stomach.

The experiments of Dr. S. W. Lewaschen prove that the carbonate, the sulphate, or the phosphate, given to dogs with biliary fistula, increase very markedly the liquidity of the bile by diminishing the percentage of solids. The salicylate of sodium acted similarly but much more powerfully than these salts. These experiments are in accord with clinical experience, which shows that the alkaline salts of soda given one to two hours after meals in full doses are of decided value in the treatment of gall-stones and various affections associated with excessive viscidity of the biliary secretion.

SODA, U. S.—*Caustic Soda* is prepared by the evaporation of the liquor, and occurs in grayish-white fragments, which deliquesce when exposed to the air; but, as the fluid absorbs carbonic acid and the soda in it is converted into an efflorescent carbonate, the liquid is after a time converted into a white powder. Caustic soda is powerfully corrosive. *Liquor Sodæ*, U.S. —*Solution of Soda.*—A colorless, exceedingly acrid liquid, containing about five per cent. of hydrate of soda, and having the specific gravity 1.059. It is made by the action of milk of lime upon a solution of the carbonate of sodium.

SODII CARBONAS, U. S.—*Carbonate of Sodium* occurs in colorless crystals, which rapidly effloresce on exposure to the air, and fall into a white powder. The taste and reaction are strongly alkaline. It is very soluble in water, insoluble in the air. The chief native materials from which it is manufactured are common salt and the sulphate of sodium. As it occurs in commerce, the carbonate of sodium is sufficiently pure for ordinary use. When the carbonate of sodium is heated, its water of crystallization is driven off, and the officinal *Dried Carbonate* (*Sodii Carbonas Exsiccatus*, U. S.) is left. This may be given in pill-form. *Commercial Bicarbonate of Sodium* (*Sodii Bicarbonas Venalis*, U. S.) is a white, opaque powder, containing variable amounts of soda not fully saturated with carbonic acid. *Pure Bicarbonate of Sodium* (*Sodii Bicarbonas*, U. S.) should always be selected for internal use. The antacid dose of these preparations is ten to twenty grains.

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* See Bernard's *Physiologie Expérimentale*, t. ii. p. 393, also *Phila. Med. Times*, vol. v., and for a discussion of the subject, Prof. F. G. Smith's note to the American edition of *Marshall's Physiology*, p. 530; also Longet's *Physiologie*, Paris, 1861, t. i. p. 196.

Therapeutics.—The fact that soda, in moderate amount, has no depressing action, and indeed very little, if any, influence upon the general system, renders it preferable to potash in cases of acidity of the primæ viæ. It is *par excellence* the alkali for acid dyspepsia. On the other hand, the circumstance clearly established by Dr. Roberts (*Urinary and Renal Diseases*, Am. ed., 1866, p. 240), that it is less powerful as a solvent of uric acid than its sister alkali, together with the property, believed to belong in a much greater degree to potash, of preventing the formation of uric acid, makes soda of very inferior value in *uric acid gravel* or *uric acid diathesis*. When in any case it is desirable simply to render the urine alkaline, and at the same time to avoid depressing the system generally, soda would, on theoretical grounds at least, seem preferable.

Sodii Acetas, U. S.—*Acetate of Sodium* is a white, slowly efflorescent salt, which occurs in long prisms of a sharp, bitterish taste. It has been supposed to have the same remedial powers as the acetate of potassium; but this is certainly a mistake. It is rarely if ever used in medicine. *Nitrate of Sodium*, although officinal, is not used as a therapeutic agent.

CALX—LIME.

The therapeutic properties of slaked lime are dependent chiefly upon its alkalinity and its astringency. It does not possess the latter property in an eminent degree, yet its preparations, when properly diluted, whiten and lessen the secretion of mucous membranes to which they are applied. It also appears to have, as it were, a sedative influence upon mucous membranes, lessening their irritability. *Caustic* or *unslaked lime* is a powerful caustic, but, except in the form of Vienna paste, is rarely if ever used as such. It is more soluble in cold than in hot water. At 60° F. it requires about seven hundred times its weight of the liquid to dissolve. It is much more soluble in syrup than in pure water.

Liquor Calcis, U. S.—*Solution of Lime.*—*Lime-water* is a colorless liquid, having the sp. gr. 1.0015, and containing about 0.15 per cent. of lime. It has an alkaline taste, and is nearly destitute of irritant properties. On exposure to the air it becomes turbid, or forms a crust upon the surface, or deposits a precipitate, owing to the absorption of carbonic acid from the air and the conversion of the lime into a carbonate. Twenty minims of *syrup of lime* (*Syrupus Calcis*, U.S.) equal a fluidounce of lime-water.

Therapeutics.—Lime-water is used internally exclusively for its effects upon the primæ viæ. In *vomiting*, from almost any cause except acute gastritis, equal parts of it and milk afford an elegant, simple, and much-used remedy. If the vomiting be severe, all other food should be inhibited, and one or two tablespoonfuls of the mixture be given every half-hour; the quantity, as well as the proportion of milk, being increased as the stomach is able to bear it. As lime-water when put in milk prevents the formation of dense coagula, it is often added with advantage to that fluid when used as food for infants, or for adults with weak digestion. As an alkaline astringent, the *syrup* is often useful in *diarrhœa* in doses of one to two fluidrachms well diluted.

Externally, lime-water has been used as a wash in various skin diseases, especially in *tinea capitis:* it is also applied to *ulcers*, and is said to have a very marked influence in lessening the amount of discharge. When mixed with an equal bulk of linseed or olive oil (*Linimentum Calcis*, U. S.), lime-water is a favorite application for recent burns: the thick, soapy liquid which is formed is sometimes spoken of as *Carron Oil*, from the name of the iron-works at which its reputation was first made.

Lime-water has the power of dissolving mucus, and also false membrane, and has therefore been introduced as a local remedy in *pseudo-membranous croup* and in *diphtheria*. It is sometimes used by causing the patient to inhale the vapors of slaking lime; but a better method is to pulverize lime-water by means of an atomizer, and direct the spray upon the back of the fauces while the patient is respiring deeply. The application should be made every two or three hours, and, in patients of sufficient age to allow of its being thorough, is often very serviceable.

CARBONATE OF CALCIUM.

Chalk is the native, friable carbonate of calcium, a milk-white, soft solid, of an insipid, earthy taste; insoluble in water; wholly soluble, with effervescence, in dilute muriatic acid. *Creta Præparata*, U. S.—*Prepared Chalk* is chalk freed from impurities by pulverization, levigation, and elutriation; a white, perfectly smooth powder. *Calcii Carbonas Præcipitatus*, U. S.—The *Precipitated Carbonate of Calcium* is a white powder, free from grittiness, which is made by precipitating chloride of calcium with carbonate of sodium.

THERAPEUTICS.—Carbonate of calcium in its different forms is used internally as an antacid and very mild astringent. As none of the salts which it forms are purgative, it, with the other preparations of lime, is the best antacid when diarrhœa is present. The crude chalk should never be used, but the other preparations are probably of equal value. Some practitioners claim, however, that the oyster-shell is more acceptable to delicate stomachs, on account of the animal matter which it contains; and, under the name of *Castillon's Powder*, a mixture of salep, tragacanth, sago, āā three parts, prepared oyster-shell one part, and cochineal q. s. to color it, has been much used in obstinate summer diarrhœas. A drachm of this is boiled in a pint of milk, and the decoction taken as food *ad libitum*. The dose of carbonate of calcium is twenty grains to a drachm. *Chalk Mixture* (*Mistura Cretæ*, U. S.) is generally preferred to the powder. It contains thirty grains of the chalk to the ounce, and is given in doses of one to two tablespoonfuls. It is often combined with laudanum or paregoric and tincture of kino or catechu.

Externally, prepared chalk and the precipitated carbonate of calcium are used as desiccants and protective applications to *ulcers* and *chronic burns;* also in *excessive sweating* of the feet, and in *intertrigo* and other affections of the skin.

CLASS II.—ANTHELMINTICS.

These are medicines which kill or cause the expulsion of intestinal worms. They are sometimes divided into *vermicides*, those which kill, and *vermifuges*, those which expel; but there is little or no practical use in the division. It is of much greater importance to establish the relations between these drugs and the different species of entozoa, since clinical experience has demonstrated that an anthelmintic very efficient against one form of intestinal worm may be not injurious to another species. Therapeutically considered. the entozoa may be divided into the *Tapeworms* (*Tæniæ*), *Round-worms* (*Lumbrici*), and *Seat-worms* (*Ascarides*). The last of these differ from the others in that they are to be attacked solely by enemata.

It is obvious that the value of an anthelmintic depends not only upon its power of poisoning the articulate, but also upon its harmlessness as regards the patient. Thus, it is the eminent combination of these qualities which renders the infusion of quassia so valuable in cases of seat-worms, whilst carbolic acid, though very efficient, should never be used against the same parasite, since it has greatly imperilled, if it has not destroyed, the life of the patient when so employed.

There are certain general rules which govern the administration of anthelmintics, and which should not be lost sight of. They may be summed up as follows: Let the alimentary canal be as empty as possible, so that the drug may act with the greatest force upon the enemy. For this reason, anthelmintics are best administered early in the morning; and in obstinate cases the patient should be required to fast until dinner-time.

If the drug be not itself a purgative, from four to eight hours after its administration a brisk cathartic should be administered; or a purgative dose of calomel may be combined with it, as the bilious purging induced by the latter drug seems to be especially obnoxious to the entozoa.

SPIGELIA—PINKROOT. U.S.

The root of Spigelia Marilandica, a herbaceous perennial, growing in the Southern and Southwestern United States. It consists of a knotty head, with numerous fine, crooked, branching rootlets. The odor is faint and peculiar; the taste sweetish and slightly bitter. It contains, according to the analyses of M. Feneulle and of R. H. Stablen, tannic acid, fixed and volatile oils, resin, and a bitter uncrystallizable body; but exactly upon what its virtues depend has not been determined.

PHYSIOLOGICAL ACTION.—Although there is sufficient testimony to show that pinkroot possesses decided narcotic powers, yet its action has been scarcely at all investigated The observations of Drs. Hodge Thompson (Inaug. Dissert., quoted by Eberle), Eberle (*Materia Medica and Therapeutics*, vol. i.), and Spalsburg (*Boston Med. and Surg. Journ.*, 1855) have shown that in overdose it causes symptoms similar to those produced by one of the mydriatics. They are acceleration of the pulse, dilatation of the pupils, heat and dryness of the skin, flushing and a swollen appearance of the face, with, in Eberle's cases, talkative delirium. Two fatal cases* of poisoning by it are said to have been recorded by a Dr. Chalmers.

THERAPEUTICS.—Spigelia is a most efficient remedy in cases of the round-worm, and is, when given within the bounds of moderation, entirely safe. It appears to narcotize the worm, and requires the use of a brisk cathartic. The *fluid extract* (*Extractum Spigeliæ Fluidum*, U. S.) is efficient in doses of two fluidrachms. A better preparation is the *Fluid Extract of Spigelia and Senna* (*Extractum Spigeliæ et Sennæ Fluidum*, U. S. 1870), which is much liked by children on account of its agreeable taste. The dose, for an adult, is f℥ss; for a child two years old, fʒss to fʒi, repeated every four hours until it purges.

AZEDARACH, U. S., the bark of the root of Melia Azedarach, or Pride of China, is used in the South as a remedy for the round-worm. It is said to possess poisonous properties similar to those of spigelia, yet it is affirmed that animals and children eat its fruit with impunity. It is usually given in decoction (℥ii to Ojss, boiled to a pint), the dose being for a child a tablespoonful every two or three hours, until the bowels are affected.

CHENOPODIUM, U. S., or *Wormseed*, is the fruit of Chenopodium anthelminticum, or Jerusalem Oak, a rank, odorous plant, growing about waste places in the suburbs of towns in the United States. It consists of minute, globular, light-brown seeds, about the size of a pin's head, of a nauseous odor and pungent taste, due to the volatile oil which they contain in large quantity. *Wormseed Oil* (*Oleum Chenopodii*, U.S.) is of a light-yellow color, becoming darker and less fluid by age, of a peculiar powerful odor and a hot burning taste.† It has been used in *hysteria*, but is now employed

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[*] These cases appear to have been indefinitely copied, and are of doubtful authenticity.

[†] In the *Maryland Med. Journal*, vol. iv. page 20, Prof. T. R. Brown reports a case in which death was attributed to the taking of an ounce or more of wormseed oil in divided doses. The patient was found in bed, unconscious, with vomited matters over his surroundings, after some hours became sensible, relapsed an hour or two later into heavy sleep, was again roused, and whilst playing cards became aphasic, deaf to conversation, acutely sensitive to other sounds, and finally died with hemiplegic apoplexy. It is plain that the wormseed was not the direct immediate cause of all these symptoms or of the fatal result.

only as an anthelmintic against the lumbricus, and more rarely the tapeworm. It is very efficient, and ten drops of it on sugar may be given to a child three years old, before breakfast, dinner, and supper, for two days, followed by a brisk purge.

Brayera, U. S., or *Koosso,* is the dried flowers and unripe fruit of Brayera anthelmintica, a tree, native of Abyssinia. They occur in compressed greenish-yellow clusters, of a fragrant balsamic odor and a taste which in a little while is acrid and disagreeable. Koosso contains a volatile oil, tannic acid, and a resin, *Koossin* or *Taeniin,* discovered by Pavesi. This is crystalline, white or yellowish, slightly soluble in water, freely so in alcohol, and was shown by Dr. Bedall (*Sydenham Year-Book,* 1868, p. 476) to be the active principle of the drug, which yields about three per cent. of it. Brayera is a most efficient remedy against the tapeworm, and even in large doses causes no greater inconvenience to the patient than some nausea, abdominal pain, and looseness of the bowels. It is generally not necessary to administer any purgative with it, and the worm is discharged dead with the last watery passages. A half-ounce of the powdered flowers is given suspended in water (*Infusum Brayeræ,* U. S., ℥ss to Oss) in the morning, with the usual precautions as to diet, or from twenty to forty grains of koossin, wrapped up in a wafer, may be substituted for the crude drug. The *fluid extract* (*Extractum Brayeræ Fluidum,* U. S.) is also efficient in doses of half a fluidounce. Care should be exercised in administering brayera to pregnant women, as it is stated that it has produced abortion.

SANTONICA—SANTONICA. U. S.

Levant Wormseed consists of the unexpanded flowers and peduncles of Artemisia Contra, a composite of Asia Minor and other parts of the East. It consists of pale, greenish-brown, smooth heads of four or five tubular flowers, of very strong aromatic odor when rubbed, and a bitter disagreeable taste. It contains volatile oil, resinous matter, and a crystalline principle, *Santonin* (*Santoninum,* U. S.), or *Santoninic Acid,* which occurs in colorless, pearly, four-sided, orthorhombic tables, soluble in from four thousand to five thousand parts of cold and two hundred and fifty parts of boiling water, freely soluble in alcohol and chloroform, moderately so in cold ether; insoluble, or nearly so, in glycerine. It has a neutral reaction, but unites with alkalies to form salts, and hence is freely soluble in alkaline solutions. When slowly heated, it sublimes, unchanged, at from 165° to 175° C. When rapidly heated, it is converted into a brownish-red oil, which becomes carmine-red upon the addition of caustic potash. On exposure to sunlight, or, more slowly, even in the ordinary daylight, the colorless crystals of santonin acquire a golden-yellow tint. If this change be a chemical and not a mechanical one, the alteration must be very slight, since, according to Krauss, the yellow crystals conduct themselves in their chemical relations precisely as do the colorless crystals, and are precipitated, by the addition of acid to their alkaline solutions, as colorless crystals.

Physiological Action.—Santonin is said to have been first introduced into medical practice in 1830, by Dr. Alms, by whom and Dr. Kahler it was simultaneously discovered. It is at present used almost solely on account of its poisonous action upon entozoa, but certainly has a very great influence upon man and the higher animals. When it is given to dogs and rabbits in large doses it causes accelerated breathing, slowing of the pulse, universal trembling, cramps, free salivation, unconsciousness, convulsions, dilated pupils, and death. (See experiments of—Manns, *Das Santonin*, Marburg, 1851; Rose, *Virchow's Archiv*, Bd. xvi., 1859; T. Krauss, *Ueber die Wirkungen des Santonins und Santonin-Natrons*, Inaug. Diss., Tübingen, 1869.) After death the lesions are not absolutely constant, but hyperæmia of the nerve-centres and congestion of the lungs and heart are nearly always present. According to Rose, dogs will recover after doses of from thirty to sixty grains, although five to six grains will produce very decided symptoms; and according to Krauss, thirty grains are required to kill a rabbit, even when they are dissolved in chloroform and given subcutaneously.

The symptoms caused by large doses of santonin in man are closely similar to those which it produces in the lower animals. There are several fatal cases of poisoning by it on record. A child five years old was killed in half an hour by an unknown quantity (*Pharm. Journ. and Trans.*, viii. 996), and one six or seven years old is said to have been destroyed by six grains of the acid, after suffering from hæmaturia* (*Bull. Thérap.*, lxxiv. 362): four grains produced very serious symptoms in a child four years old (*Pharm. Journ. and Trans.*, ix. 696). In Dr. Grimm's case (*Schweizer Zeitschrift für Med., Chir., und Geburtshilfe*, 1852, p. 493), a rather feeble child, five years old, took two one-grain doses of santonin, and was seized with convulsive tremblings, which increased in severity until they became severe convulsions, which were accompanied by unconsciousness, trismus, pallor of the face, cold sweats, dilated pupils, and rapid pulse and respiration. Thirteen or fourteen hours after the ingestion of the poison, whilst the patient lay on her back, quiet, unconscious, with moderately-dilated pupils and a slow, feeble pulse, death occurred suddenly. No post-mortem was allowed. The santonin is said to have been chemically pure and to have been used in other cases with its usual results. Nine-tenths of a grain of santonin are said to have caused complete unconsciousness in a child five years old (*Schmidt's Jahrb.*, Bd. cci. 128). In quite a number of very serious but not fatal instances of poisoning the symptoms have been similar to those in the case just detailed; great pallor of surface, with a blue color around the eyes or involving the whole countenance, has been generally an early symptom; vomiting has not rarely been present, and sometimes has been accompanied by colicky pains. Besides these manifestations, giddiness, mental apathy or stupor, great coldness of the surface, profuse sweating, trembling, mydriasis, and finally loss of consciousness, with convulsions, often violent and accompanied by opisthotonos and emprosthotonos, and failure of respiration, are the usual phenomena of santonin-poisoning. The circulation seems to be very little affected (case, *Arch. Exper. Pathol. u. Pharm.*, vi., p. 302).

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* This is probably a mistaken observation, the urine being only blood-colored, and not containing blood (see p. 603).

A very curious symptom caused by santonin, even when in doses which can scarcely be called toxic, is xanthopsia, or "yellow-seeing," as the Germans term it. It was, I believe, first noticed by Calloud, and has since been spoken of by almost every writer upon the drug. Usually it consists of a very deep yellow tint imparted to the landscape and to every object looked at, an effect perhaps most comparable to that of looking through yellow glass; sometimes this yellow is replaced by green; and Heydloff states that he has seen patients in whom the tint was red, and others in whom it was blue. Dr. Edm. Rose has published exceedingly elaborate papers upon this chromatopsia; but, as the matter is of interest rather to the physicist and student of optics than to the clinician, I content myself with a reference to his memoirs, which may be found in *Virchow's Archiv* (xvi. 233; xviii. 15; xix. 522; xx. 245; xxviii. 30). Santonin is eliminated probably in a more or less altered condition by the kidneys, and thus gives rise to a very characteristic symptom or sign of poisoning by the drug which has not as yet been spoken of,—namely, discoloration of the urine. The new color is a very marked yellow, which has at first an orange tint, but after very large doses becomes saffron-like, or sometimes even a purplish red, which has given origin to the idea that blood was present. According to Manns, the addition of an alkali to the yellow urine causes it to become red. The exact nature of the eliminated principle has not been determined: it is, however, probably the result of an oxidation of the santonin, as is believed by Kletzinsky, who asserts that the drug receives in the system six atoms of oxygen.

The results of the ingestion of large doses of santonin show that it has a very powerful action on the organism; but as to what portions of the latter are especially affected we have no information. Rose believes that the chromatopsia is due to a peculiar action of the drug upon the nerve-centres; but it seems to me more probable that it is simply the result of a very faint staining of the humors and other parts of the eye by the drug, and is analogous to the similar phenomenon sometimes seen in jaundice. Like very many other substances which escape through the kidneys, santonin increases the flow of urine, and, according to Dr. Farquharson (*British Medical Journal*, 1872), increases slightly the elimination of urea.

THERAPEUTICS.—Dr. D. Dyce Brown (*Brit. and For. Med.-Chir. Rev.*, April, 1871), having noticed that a blind man to whom he was giving santonin for worms recovered to an extraordinary degree his vision, has recommended it in cases of loss of optic nerve power, and Dr. Ogston has used it with more or less complete success in a number of cases. Although Dr. Brown had apparently no knowledge of it, yet many years before his experience M. Guépin and M. Martin recommended the drug in *amaurosis* (*Ann. de Thérap.*, 1862). M. Guépin believes it to be especially useful in amaurosis following choroiditis and iritis. Whether the use of santonin in diseases of the eye will or will not ever amount to anything, cannot at present be told; but in the past the drug has been employed almost solely as an anthelmintic in persons troubled with the *lumbricoid* or *round worms.* It is a parasiticide, killing and not expelling the worm, and consequently should, when used, be combined with or followed by a brisk cathartic. Especial advantage is said to be derived from the joint use of it and calomel. It has been employed in *epilepsy* (*Brit. Med. Journ.*, 1876, ii., p. 787).

TOXICOLOGY.—It has been denied that santonin is poisonous, and asserted that the evil results which have followed its use have been due to the mixture of strychnia with the drug. The only ground for this opinion is that in one or more cases death has resulted from strychnia being mixed with santonin, or else sold instead of santonin (*Lancet*, 1877, ii., p. 857), through the carelessness of an apothecary. Dr. Walz, in an extended examination (*Jahresbericht für Pract. Pharmacie*, Bd. xv.), found that the santonin of the shops is pure; and it is inconceivable how strychnia could be mixed with it except purposely or by the grossest carelessness. Moreover, the symptoms which have been produced in alleged poisoning by santonin are very different from those caused by strychnia, and are in close accord with those which santonin induces in the lower animals. Finally, in some of the reported cases, seven of which are collected by Krauss, the santonin was examined and found to be pure. Under these circumstances, it would be absurd longer to deny the poisonous properties of santonin. The reason large doses have been so often given without serious results is probably the great hardness and insolubility of the crystals of the drug. The treatment of poisoning by santonin, after evacuation of the stomach and bowels, must at present be entirely tentative. One case appears to have been saved by artificial respiration (*Arch. Exp. Path. u. Pharm.*, vi., p. 300); but Prof. Binz (*Ibid.*) has found in animals nitrite of amyl, morphia, and artificial respiration alike useless; chloral given before the poison he found of service.

ADMINISTRATION.—Santonin is best administered in the form of lozenges, which, if the unbroken crystals are used, can be rendered very pleasant to the taste, so that children will eat them as candy. The dose of santonin for an adult is two to four grains; for a child two years old, one-fourth to one-half grain. Very alarming symptoms have been caused by two one-grain doses exhibited within three hours in a child eight years old (Grimm); in a child two and a half years old, four grains apparently came very near causing death (Dr. Berg, *Württemberg. Medic. Correspondenzblatt*, 1862); and in the fatal case noted on page 573, only two grains were taken by a child five years old.

For young infants, santonin is hardly a safe remedy in any efficient dose. When a dose of any size is given, it should not be repeated in less than eight hours, and the last dose should be accompanied by a purgative amount of calomel.

The *santoninate of sodium* (*Sodii Santoninas*, U. S.) has been proposed instead of santonin, but as an anthelmintic it is much more dangerous and less efficient: the object is to get as much of the remedy as possible in contact with the worm, and as to do this a slow, not rapid, absorption is necessary, the insolubility of santonin is an advantage.

ASPIDIUM, U. S.—*Filix Mas*, or *Male Fern*, is the rhizome of Aspidium filix mas, or male fern of Europe. Under the name of Aspidium the present U. S. Pharmacopœia recognizes it and the rhizome of the indigenous A. marginale. The rhizome, when perfect, is six to twelve inches long, and covered with large, brown, imbricated scales. Its taste is bitter and astringent. Its therapeutic properties appear to reside in an *oleoresin* (*Oleoresina Aspidii*, U. S.), which, as extracted by means of ether, is a dark, thick liquid, of a bitterish, nauseous, slightly acrid taste. Male fern is employed almost exclusively against the *tapeworm*. In its administration it is necessary to regard strictly the general rules applying with greater or less force to all the remedies of the class, which are especially imperative when a drug is employed against the tapeworm. The patient should live upon milk and a little bread for one day, and the following morning take a full dose (fʒss to fʒi) of the oleoresin, fasting, and repeating it in two or three hours. At noon the patient may resume the use of food, and in the evening a brisk cathartic should be given. In overdoses male fern acts as a violent intestinal irritant, and six drachms of the oleoresin have caused death in the adult (*Lancet*, Oct. 14, 1882).

PEPO, U. S.—*Pumpkin Seeds.*—The seeds of the ordinary pumpkin are a most valuable remedy in cases of *tapeworm*, perhaps even more efficient than the male fern, and perfectly harmless. Two ounces of the seeds may be beaten up with sugar into an electuary, or with water into an emulsion, and be taken fasting in the morning, the patient having dieted the previous day. Some hours after their administration, a brisk purge should be given. Mr. I. G. Wolff asserts that the active principle is a resin, which he has found efficient in doses of fifteen grains.

TURPENTINE, in doses of half a fluidounce, has been used in cases both of *tapeworm* and of *round-worm*. It is efficient, but is liable to produce unpleasant effects, and should be employed only when other remedies have been used without success or are not to be had. It should be given in combination with twice its bulk of castor oil.

GRANATUM, U. S.—*Pomegranate Rind.*—The bark of the pomegranate root is efficient, though very unpalatable, against the *tapeworm*. The decoction of the fresh root (℥ii to Oj) is to be preferred; a pint of it to be taken in three doses, an hour apart, before breakfast. The French chemist C. Tanret has isolated from the bark four alkaloids (*Bull. de Thérap.*, xcviii. 316), of which two, *pelletierina* and *isopelletierina*, have been found by Dujardin-Beaumetz to be active tæniacides. In sufficient amount it is stated that they act in the same manner upon the higher animals as does curare, causing paralysis of the motor nerves, without affecting sensation or muscular contractibility (*Ibid.*). The dose of the salts of the alkaloids is said to be 4.6 grains. The efficiency of pelletierine as an anthelmintic has been confirmed by various clinicians. It has by some been used in doses of twenty grains. Dujardin-Beaumetz also has employed it successfully in Ménière's disease, and states that hypodermic injections of six grains produce in man severe vertigo and muscular weakness with great retinal congestion.

MUCUNA.—*Cowhage.*—The sharp, rigid hairs of the pods of Mucuna pruriens, an East India plant, were formerly used in cases of the *roundworm*. They are believed to kill the worm by piercing it. The pods are dipped into molasses, the hairs scraped off, and a tablespoonful of the thick mass given to an adult—a teaspoonful to a child—morning and evening, for three days, after which a brisk purge is administered.

KAMALA, U. S.—*Kamala.*—The hairs of the fruit of Rottlera tinctoria, a plant cultivated in India as a dye-stuff. It is said to be an efficient parasiticide in cases of *tapeworm*. It is an orange-red, very inflammable, granular powder, mixing with water with some difficulty, and containing traces of a volatile oil and coloring resinoids. to one of which Dr. Anderson has given the name of *Rottlerin*. Kameela, in full doses, is actively purgative, indeed drastic, and sometimes causes also nausea and vomiting. It imparts its virtues to alcohol, and hence may be exhibited in the form of tincture. The dose of the powder is from one to two drachms suspended in syrup, given in the morning, and repeated in eight or ten hours if it do not purge.

CLASS III.—DIGESTANTS.

In this class are put a few remedies which are used to aid the stomach in dissolving the various articles of food. There are, I think, really but three articles worthy of a position in the class: namely, pepsin, hydrochloric acid, and lactic acid. Prof. Geo. B. Wood claims, however, a position in it for *yeast*. The theory upon which the latter drug is employed is that in *diabetes* there is an excessive formation of sugar in the stomach, and that the yeast, by causing a fermentative alteration of this into acetic acid, will do good. With our present knowledge of the pathology of the disorder, it is certain that the sugar is not formed in the primæ viæ, but in the liver, or at least in some internal viscus; and, this being so, it is evident that the theory above spoken of falls to the ground. Further clinical experience has, I think, demonstrated the uselessness of yeast in diabetes, and at present the remedy is very rarely, if ever, exhibited in that disorder.

PEPSINUM SACCHARATUM. U.S.—PEPSIN.

As every one knows, there is secreted by the gastric glands a peculiar albuminous body, which has the power not only of coagulating albumen, but also, with the aid of acidulated water, of redissolving it. To this principle the name of pepsin has long been given. A discussion of its nature and properties would be more in place in a work upon physiology than in one on therapeutics, and I shall therefore say nothing further about them.

The dried stomach of calves has been used since time immemorial for the purpose of coagulating milk, by housewives, with whom it is customary to place the dried viscus in wine, and to call the liquid thus formed, as well as the prepared stomach, *rennet*. It is stated by Dr. Jas. Gray (*Edinburgh Med. Journ.*, Jan. 1853) that rennet-wine should be of such strength that one teaspoonful of it will coagulate a pint of milk. Rennet is said to have been long used in England as a domestic remedy in dyspepsia (*Med. Times and Gaz.*, April, 1857). In South America, the inner coat of the gizzard of the ostrich is stated to be put to a similar use (E. S. Wayne, *American Journal of Pharmacy*, 1868); and in our own country the dried gizzards of chickens and turkeys are no less famous among medically-inclined housewives.

Dr. Corvisart, of Paris, is asserted to have been the first to propose the use of the active principle of the stomach in feeble digestion; and of latter years the manufacture and consumption of pepsin have become very great. Various processes have been suggested for the preparation of the drug, but none of them yield a pure proximate principle, if indeed pepsin have really such nature, and be not an albuminous body of varying constitution. By most of the methods of manufacture the pepsin is obtained in the form of a viscid fluid; and to change this into a powder requires the addition of a large quantity of starch or sugar, so that the powdered pepsin, as sold. contains a considerable percentage of foreign material.

Whatever form of pepsin be used, if good effects are to be obtained from it it must be given with acid, unless indeed there be reason to believe that this constituent of the gastric juice is not wanting. Alcohol destroys the digesting power of pepsin, and therefore wines are inferior preparations of it. The reactions of pepsin with organic and inorganic matters are very complex, and not well understood: consequently I think the physician should eschew all elixirs or compound preparations of the drug, using only the powdered pepsin or a glycerole of pepsin, or a freshly-prepared digestive solution. If other remedies are to be given, it is no great hardship to write a second prescription and exhibit them by themselves. In making the digesting fluid, water and muriatic acid, or glycerine, water, and muriatic acid, should alone be employed with the pepsin.

THERAPEUTICS.—It is a question of some importance to decide how far pepsin is valuable and reliable as a medicine. It is evident that any influence for good which it possesses is dependent upon its solvent power, and that this, therefore, is a measure of its value. According to the experiments of Dr. C. L. Dana, which seem to be very reliable, good pepsin ought to dissolve in the stomach twenty times its weight of albumen and the U. S. Pharmacopœia requires that the pepsin, aided by hydrochloric acid, should dissolve fifty times its weight of coagulated egg albumen in five or six hours; but it is very doubtful whether twenty per cent. of commercial pepsin will do this. One of two conclusions seems to be inevitable: either the doses of pepsin habitually used are preposterously small, or else pepsin acts upon the stomach itself in some way as a stimulant. Clinically, pepsin has been used with asserted advantage in the *loss of digestive power* in adults, whether primary, or occurring in the course of other affections. Probably four-fifths of the drug which has been given has been inert, either originally or from the method of its administration; and in the great majority of cases the good that has been achieved has been probably due, not to the pepsin, but to the regulation of the diet and habits of the patient and to the drugs which have been exhibited along with the animal ferment. The value has been over-estimated, and it has been given to adults in ridiculously small doses: at least half a drachm of the commercial article should be given at a dose. The testimony as to the value of pepsin in diseases of young children is very strong. To such it is generally given in doses nearly as large as those usually exhibited in the cases of adults. If we represent the absolute digesting power of ten grains of pepsin as x, it is evident that x represents a proportionately much greater power in the primæ viæ of a child than in those of an adult. The use of pepsin in children is therefore much more rational than in adults; and my own experience is in close accord with what seem to me the dictates of common sense: in the *chronic indigestion* and consequent *diarrhœa* of young children it may be tried with great hope of benefit. To a baby six months old five grains may be given in a little acidulated water after each feeding.

Pancreatin.—Modern physiology has shown that the pancreatic secretion has varied and extensive digestive powers, and *pancreatin*, *pancreatic extracts*, and other similar products are now found in commerce. They have been especially commended by Dr. Wm. Roberts (*On the Digestive Ferments*, London, 1881). There are two ferments in the pancreatic fluid, *pancreatic diastase*, which dissolves starch, and *trypsin*, which is closely allied to pepsin in its activities. When milk is subjected to pancreatic digestion in the presence of an alkali, it becomes first softly curdled, then the curds dissolve wholly or in great part, and the fluid assumes a peculiar, characteristic yellowish-gray color, and acquires a peculiar, bitterish, to most persons unpleasant taste. It is now peptonized, and is not coagulated by nitric acid or by boiling.

If pancreatin be added to fresh milk without an alkali, in the course of a few minutes the liquid acquires the property of curdling abundantly upon boiling; and Dr. Roberts takes advantage of this fact as a means of testing the activity of a pancreatic preparation. The value of a sample is estimated as the number of cubic centimetres of milk which are transformed to the curdling point in five minutes by one cubic centimetre of the sample at a temperature of 40° C. The *liquor pancreaticus* used by Dr. Roberts has a power oscillating between fifty and seventy. In applying his processes for peptonizing milk this must be remembered, and the amount of pancreatin used made to correspond. *Peptonized milk* is made by diluting a pint of milk with a quarter of a pint of water, heating to about 140° F., adding two teaspoonfuls of the liquor pancreaticus with twenty grains of bicarbonate of sodium, digesting in a warm place for an hour to an hour and a half, and raising momentarily to the boiling point; at the temperature of the sick-room, 65° F., the digestion will usually require about three hours. *Peptonized milk gruel* is especially commended. It is made by first preparing a thick gruel with arrowroot, oatmeal, sago, or other similar farinaceous articles; whilst still hot, an equal quantity of milk is added, the mixture to have a temperature of 125° F.: to each pint are added twenty grains of the bicarbonate and two teaspoonfuls of the liquor, digestion allowed in a warm place for two hours, and the mixture momentarily boiled, and then strained. *Peptonized beef-tea* is prepared by simmering half a pound of minced beef for two hours in a pint of water containing twenty grains of bicarbonate of sodium, allowing to cool to about 100° F., digesting at this temperature with a tablespoonful of liquor pancreaticus for three hours, decanting, and momentarily boiling. This beef-tea is said to be about equivalent to milk in nutritive value, containing 4.5 per cent. of organic solids, three-fourths of which is peptone.

The following recipes, which were devised by Dr. N. A. Randolph, are said to yield very good results:

1. *Pancreatized Oysters.*—The oysters of an ordinary stew (containing milk) are removed and finely minced, then returned to the liquid portion of the stew. The whole is brought to a temperature of 100° F., the appropriate proportions of pancreatic extract and sodium bicarbonate are added, and the mixture maintained at the temperature mentioned for thirty minutes, with occasional stirring. It is then strained and served, and forms not only a highly nutritious and palatable soup, but one which is retained by very irritable stomachs, and utilized with a minimum of digestive power. After boiling, to prevent the further action of the digestive ferment, gelatine may be added, and the mixture served cold, as a jelly. Cooked tomato, onion, celery, or other flavoring suited to the individual taste of the patient, may be added at the beginning of the artificial digestion, and the solid residue removed in the final process of straining, at which time it will be noticed that the minced oysters originally added have been in great part dissolved.

2. *Pancreatized Milk-Toast.*—Ordinary milk-toast, in which there is an abundance of milk, when digested in the manner just described, becomes an almost homogeneous, pulpy mass, which, when the crusts have been removed, is usually acceptably retained by the irritable stomach. In extreme cases, however, it may advantageously be strained and the fluid portion alone used, in which the partially peptonized solution of casein of the milk is reinforced by actually digested gluten and starch of the bread, together with a very little dextrin. Plain, light sponge-cake may be similarly digested, and occasionally forms a desirable change.

Pancreatin has also been used extensively as a therapeutic agent in dyspepsia. Its value is, however, problematical. For action it requires the presence of an alkali, and in the acid gastric juice would not only not act, but would itself in all probability be digested and destroyed as a ferment (*New York Medical Record*, xl. p. 398). Dr. J. Milner Fothergill proposes to prevent this destruction of pancreatin by administering ten to fifteen grains of bicarbonate of soda with the dose; but there is no valid reason for believing that this amount of alkali would be capable of sufficiently altering the gastric juice to allow of the escape of the pancreatin.

Feeding by the Rectum.—It is sometimes of the greatest consequence to feed a patient in other ways than by the stomach; and therefore the question of nourishing by the rectum is one of the gravest importance. The solvent influence of the rectal juices is practically nothing, and formerly the attempt was made to supplement this complete lack of power by the use of soups. It is evident that very little nutriment can be introduced into the system by such a plan; and consequently feeding by the rectum has hitherto been only a "forlorn hope," and has accomplished little good. Dr. W. O. Leube (*Deutsches Archiv für Klin. Med.*, 1872) has proposed a new plan, which bears upon its face the marks of efficiency, and which, as he has proven by experiments made upon dogs, is capable of yielding to the blood largely of nutritive materials. Moreover, he has by it maintained life for four weeks in a patient who had been poisoned with iodine and whose stomach rejected all food. The plan consists simply in digesting the food before injecting it into the rectum. The method is carried out as follows. The pancreas of swine or cattle is carefully cleaned of fat, and 50 to 100 grammes thereof cut into very small pieces. In like manner 150 to 300 grammes of beef are prepared. Both substances are then put into a dish with about 50 to 150 cc. of lukewarm water, and stirred into a thick paste, and drawn in a clyster-pipe with wide opening. In many cases from 25 to 50 grammes of fat may be added to the mixture, also at times some starch. An hour before using this clyster, one of pure water should be administered, to clean out the intestines. In very warm weather there is some trouble in obtaining and keeping sweet the pancreas. This difficulty may be avoided by making a glycerine extract, which is said to be quite equal in digestive power to the fresh pancreas, and will remain good for several weeks. The following is the manner of its preparation. The pancreas of a bullock (which is sufficient for three enemata) is finely chopped and rubbed with 250 grammes of glycerine; and to each third of this, when about to be used, are added from 120 to 150 grammes of finely-divided meat. It is important that this mass should be injected into the intestine as soon as it is made; for if it is allowed to stand, the meat swells and the operation is thereby rendered difficult. For these preparations of Dr. Leube the pancreatic beef-tea, etc., of Dr. Roberts might perhaps be substituted with advantage.

The experiments of Dr. L. S. Joynes (*Richmond and Louisville Med. Journ.*, 1869) have shown that the stomach of the pig, placed in water acidulated with hydrochloric acid, will not only rapidly dissolve itself but also small pieces of beef. When life is to be maintained by rectal feeding, probably a preparation made in this way could with advantage be alternated with the solutions of Leube.

CLASS IV.—ABSORBENTS.

This class contains remedies which are used for the purpose of absorbing acrid and deleterious materials, such as offensive discharges on the exterior of the body, and acrid secretions, or the irritant products of the partial decomposition of food, in the alimentary canal. For the first purpose very fine dry earth and plaster of Paris are used to some extent in practice; but, as their employment is purely in the province of the surgeon, I shall say no more about them here.

CHARCOAL.

Charcoal is officinal in the U. S. Pharmacopœia in two forms:

Carbo Ligni.—*Charcoal* prepared from wood.

Carbo Animalis.—*Animal Charcoal*, prepared from bone.

Charcoal for medical purposes should be made out of a light porous wood, and that prepared from the young shoots of the willow or of the poplar is almost exclusively employed. It is a black, brittle substance, and should have more or less lustre. It has a very remarkable power of absorbing many times its own bulk of gases, and, when exposed to the air, increases rapidly in weight. It should therefore, when intended for medicinal purposes, be powdered so soon as it is burnt, and put in small, completely-filled, closely-sealed bottles.

Animal charcoal, or *bone-black*, formed as it is by the partial burning of bones, contains a large percentage of the phosphate and the carbonate of calcium. Although this does not interfere with its strictly medical employment, it does with many of its uses in pharmacy; and consequently the U. S. Pharmacopœia directs that a *Purified Animal Charcoal* (*Carbo Animalis Purificatus*) be prepared by digesting ordinary animal charcoal in dilute muriatic acid, by which all the lime salts are dissolved out, washing thoroughly with water, and heating to redness.

Bone-black possesses absorbing powers far greater than those of ordinary or wood charcoal, and takes up coloring-matters, alkaloids, and other substances from these solutions: it is therefore very extensively used in pharmacy, as well as in the refining of sugar, and in other processes of the arts.

Therapeutics.—Charcoal is used externally as an absorbent and disinfectant dressing to *foul wounds* and *ulcers*. A *charcoal poultice* may be made by adding one to three drachms (according to size) of powdered charcoal to a flaxseed poultice; or, as the British Pharmacopœia directs, two ounces of bread may be well mixed with ten ounces of warm water, an ounce and a half of flaxseed meal be thoroughly stirred in, and to the cataplasm thus formed two drachms of powdered charcoal be added, and one drachm be sprinkled on the surface.

Internally, charcoal is employed as an absorbent in those cases of acute or chronic *indigestion* in which there are offensive liquids and gases in the alimentary canal, giving rise to local symptoms and foul discharges: in this way it is sometimes employed in *dyspepsia*, *cardialgia*, and similar disorders. It is at least conceivable that charcoal, given very freely, should accumulate in the alimentary canal, and mechanically cause serious trouble: for this reason, its habitual employment is very generally combined with that of laxatives.

On account of its power of absorbing alkaloids, *purified animal charcoal* has been recommended in poisoning by substances of that class. Its action is, however, too slow for much good to be expected from its use. If given at all, it should be exhibited very freely, since at least half an ounce of it is said to be required for the absorption of one grain of the poison.

ADMINISTRATION.—The ordinary dose of charcoal is from half an ounce to one ounce. Except in a mechanical way, it is perfectly innocuous in any dose

CLASS V.—DISINFECTANTS.

Disinfectants are substances employed for the prevention or destruction of noxious miasmata or effluvia. It is evident that the consideration of these materials belongs rather to the province of hygiene than to that of therapeutics, since their employment is hygienic rather than medicinal, preventive rather than curative. The importance of disinfection is, however, so great that I shall treat of it, although very briefly, and giving especial attention to the action of disinfecting drugs upon the human system. For further details the reader is referred to the classical work of Vallin and the able report of the Committee of the American Public Health Association, 1885.

All disease-poisons may be divided into those which are generated or multiplied within the human body, and those which arise solely without the body. To the former I shall apply the term "contagions," to the latter the term "miasms." Of the nature of miasms we have no definite knowledge, but it is probable that in many, if not all, cases they are organic entities. It is certainly established in regard to very many contagions that they are living forms, and for practical purposes all contagions must be considered of such nature. In the experimental study of the power of poisonous agents over the contagions, we are forced to take, as the measure of the power of such agents, the influence which they exert over the lower forms of life. We have no better criterion for judging of the effectiveness of disinfectant agents upon miasms. It must be remembered that these poisons are not necessarily connected with bad odors, but may in a most deadly form saturate the air in an apparently clean chamber, whilst the emanations from the most stinking cesspool may be free from them. It is probable, however, that foul gases are of themselves able to produce systemic depression, although not definite disease. It is, therefore, always important to prevent the giving off of foul gases from masses of decomposing matter.

An *antiseptic* is not always a *germicide*, though a germicide is always an antiseptic. The antiseptic is a substance which has the power of preventing putrefaction, that is, the growth of the organisms which produce putrefaction. Whereas the germicide is a substance which is capable of killing disease-germs and their spores, which entities are much more resistant than are the bacteria of putrefaction; thus alcohol, common salt, borax, sulphate of iron, and many other agents commonly used as antiseptics do not even in concentrated solution destroy the spores of bacilli, and consequently are not germicides.

A question of very grave importance naturally arises here, as to the exact province of disinfection when applied to contagions; or, in other words, Is it possible to destroy them in the air? It is a law which holds everywhere, that the more imperfectly developed animal organisms are, the more tenacious are they of life; also experience has shown that all substances actively poisonous to contagions are still more poisonous to the germinal matter of human beings, and that it may be laid down as a general proposition that it is impossible to destroy the contagion-germs in the confined air of a room while men or women remain in the apartment. When it comes to the general atmosphere, to attempt to disinfect it, to essay the destruction of a widespread poison, such as, for example, exists in a smallpox epidemic, is simply so childish as to need no discussion to reveal its utter futility.* It is well known that contagions diluted beyond a certain point are powerless, and the admission of large quantities of *fresh* or *pure air*, or, in other words, *free ventilation*, is the only means at our command of disinfecting rooms in which there are human beings. In ventilating an apartment, it must always be remembered that it is not merely air, but pure air, that is required. To ventilate one room into another, as is sometimes done, is foolishness; to open a window with the wind blowing over a miasmatic swamp or an open sewer, may be but to invite disease. The opportunity to destroy disease-germs is to be found not after they have been dispersed into the air, but whilst they are still in connection with the various solids and fluids passed from the body or brought in contact with it. In most, if not all, contagious diseases the poison-germs are eliminated in large quantities with the urinary and fecal discharges; it is of the most vital importance to act on the excretions so soon as they leave the body; and the disinfectant should be placed in the receptacle *before*, not after, it is used. To allow any excretion, sputum, or other infected discharge to exist for a moment undestroyed, or at least undevitalized, is most culpable neglect.

The nature of miasms is not known at all. Over many of them, malaria for example, we have no control. Those which we are able to influence are almost all the results of animal or of vegetable decomposition, either alone or conjoined. After these poisons have been produced and diffused through the air, they are probably in great part beyond our reach. The only thing that can be done is to dilute them precisely as in regard to contagions; and hence free ventilation is the only reliable disinfectant under these circumstances. The stinking gases are probably of use as indicators of the presence of more subtle poisons. The gases which arise from cesspools and similar depositories no doubt act as carriers of the peculiar poisons produced in these places, and it may be that destruction of the gas causes a deposition of the organic poison. This is, however, merely speculation: it is not proven. Moreover, the deposition of a poison in an apartment is no advantage. Even then if it were possible to make an apartment appear to the smell pure by destruction of its stinking gases no good would be accomplished by so doing. Wide-open windows, great draughts of fresh air, are the only proper disinfectants for a close room or a noisome hospital-ward. The attempt so often indulged in to purify such apartments by little saucers of chlorinated lime or of carbolic acid would be exceedingly ludicrous if it were not for the frightful results of the false security engendered.

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* For failure of such attempt, see *New Orleans Med. and Surg. Journ.*, Nov. 1875.

It is otherwise when the gases are destroyed at their places of emanation. Thus, if a sewer be belching forth deleterious gases and poison, chlorinated lime or other materials generating disinfecting gases at the mouth, or in the sewer, may really be of service by destroying the noxious vapors before they find their way out and carry with them into the air the poisonous effluvia.

Although miasms cannot be readily destroyed when once generated, yet in very many instances we have power to prevent their formation. In doing this the chief factor is *cleanliness*, and the best disinfectant is *water*. Water acts chiefly in two ways: first, by dilution; secondly, by destroying organic substances. In order for decomposition to produce serious poisoning, the mass of material must be considerable. If the matter be diffused through a large bulk of water, and this spread over a considerable surface, it is evident that the effect of dispersion is obtained. Further, when water containing organic matter is allowed to run away in its natural channels, oxidation and destruction of the impurities result. Without entering further into the subject, it is sufficiently evident that, so far as miasms, and also disease-germs in the air, are concerned, *air and water are the great disinfectants*, and that the most skilful use of chemical substances cannot take the place of ventilation and cleanliness. Moreover, antiseptics may do harm by delaying the destruction of filth by putrefaction, which latter process is simply nature's method of getting rid of filth. Destructive, that is, oxidizing disinfectants, rather than antiseptics, should be used in cesspools. On the other hand, when the contents of a privy or other organic mass has been infected by disease-germs, it is essential to kill such germs by a germicidal agent.

The most complete and thorough, but the most destructive of all disinfecting agents is *fire*. *Heat* of less intensity may be used either *moist* or *dry*. The germicidal powers of moist heat have been especially investigated by Dr. George M. Sternberg, who finds that, in the absence of spores, boiling water will quickly destroy the vitality of all micro-organisms of the class to which known disease-germs belong; that boiling for two hours does not kill the spores of Bacillus subtilis, but a more prolonged boiling is fatal; that steam at a temperature of 110° C. (230° F.) maintained for one or two minutes, or of 105° C. (220° F.) maintained for ten minutes, will infallibly destroy the spores of bacilli, the most difficult test of disinfecting power known.

In regard to dry heat, the results reached by Koch and Wolffhügel (*Mitt. Kais. Gesundtheitsamte*, Bd. i.) are in accord with our other evidence, and may be considered correct. They are as follows:

1. A temperature of 100° C. (212° F., dry heat), maintained for one hour and a half, will destroy bacteria which do not contain spores.

2. Spores of mould-fungi require for their destruction in hot air a temperature of from 110°–115° C. (230°–239° F.) maintained for one hour and a half.

3. Bacillus spores require for their destruction in hot air a temperature of 140° C. (284° F.) maintained for three hours.

4. In dry air the heat penetrates objects so slowly that small packages, such as pillows or small bundles of clothing, are not disinfected after an exposure of from three to four hours to a temperature of 140° C. (284° F.).

5. Exposure to a temperature of 140° C. (284° F.) in dry air for a period of three hours injures most objects requiring disinfection (clothing, bedding, etc.) to a greater or less degree.

Dr. George H. Rohe (*Med. News*, 1885, i., p. 283) found that rolls of blankets exposed in a chamber heated to 280° F. for three hours were very slightly affected in their interior, and it is evident that whenever clothing is to be disinfected, prolonged boiling is the surest method; and that when pillows, bedding, or articles of furniture are seriously infected, taking them apart before disinfection is essential.

LEAD AND IRON.

There are various metallic salts which are believed to act as disinfectants by uniting with the sulphur of sulphuretted gases and precipitating as sulphurets. As examples of such may be mentioned sulphate of zinc and nitrate of lead. Under the name of *Ledoyen's Disinfectant Solution*, a solution of the latter salt has been and still is used to a considerable extent as a disinfectant. Although it certainly destroys sulphuretted hydrogen with great rapidity, it does not seem to me a good material for the purposes to which it is applied. The reasons of this are, first, it has no action besides that of a desulphurating body; second, it is a comparatively dear salt; third, it forms an intensely black precipitate, discoloring everything with which it comes in contact.

The power which the *oxides of iron* have of converting ordinary oxygen into ozone has already been spoken of (p. 99). This action is a slow, persistent one, and the oxidation which results is equally slow and persistent. As already stated, organic matter, if diffused through water and exposed to the air, is gradually destroyed by oxidation. It has been found that when water which is loaded with the products of decomposition is exposed to the action of iron plates, or even of iron pipes, this destruction of organic impurities is greatly hastened. According to Mr. G. Michaelis (*Philadelphia Medical Times*, vol. iii. p. 621), even the most filthy water, under the influence simply of iron plates and the air, will become perfectly pure in forty-eight hours. The action is evidently one of oxidation, but is in its details complicated. According to the researches of Dr. Mankiwich, iron possesses the property of converting ammonia into nitric acid, and also facilitates, or even provokes, such decomposition in the organic matter as shall cause ammonia to be formed. The nitric acid thus generated is one of the most powerful oxidizing substances known, and as fast as formed attacks the organic matter. It is evident that in this process the iron acts as an intermediate agent between the air and decomposing matter; that, unlike the permanganate of potassium, it does not itself undergo a conversion equivalent in chemical relation to the oxidation, and consequently that its power is not so limited as that of those compounds. The iron, however, undoubtedly suffers to some extent, and is largely oxidized; but the oxide formed has certainly the power of generating ozone, and very probably to as great an extent as the original metal. How soon the power of oxidation is finally lost, and what eventually becomes of the iron, in the presence of an overwhelming mass of organic matter, has not, that I am aware of, been determined.

COPPERAS, or *impure sulphate of iron*, is an important destroying disinfectant, although, according to recent experiments, it has no germicidal power.* The changes wrought by sulphate of iron thrown into a mass of decomposing matter are very complex and not absolutely known. In the first place, if sulphuretted hydrogen and ammonia be present, a sulphuret of iron is at once precipitated; again, a part of the salt is decomposed by the ammonia, and probably also by the stinking alkaloids which exist in the decomposing mass of a cesspool; further, by oxidation, in all probability, some of the protoxide of iron is changed into the sesquioxide, by which the ozonizing power of an iron compound is doubtless exerted long after the destruction of the original salt. The sulphuric acid set free from the iron very probably contributes to a feeble extent in the destructive reactions which are set up. From what has been already stated, it is evident that the sole use of the copperas is in altering the course of putrefaction and in destroying its products.

If a rapid effect be desired, or a mass of solid material is to be acted on, the copperas should be in solution; if a more persistent action is wanted, or if the mass is liquid, the method employed by Eckstein, of using a parchment sack, may be resorted to, or the salt in powder may be scattered over the surface of the material to be disinfected.

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* That this substance is of great practical value for use in cesspools, etc., is strongly indicated by the experiments of Albert Eckstein, who published (*Zeitschrift des Oester. Apotheker-Vereines*, Feb. 10, 1873) an account of his attempts to disinfect a privy which was used daily by one hundred persons: 1. Two pounds of the sulphate of iron in solution were used. After from two to three hours all bad smell had disappeared, but in twelve hours all the influence of the disinfectant was lost. 2. The sulphate of copper was employed in solution; result the same. 3. Two pounds of the sulphate of iron in crystals were thrown in; their effects lasted two days. 4. The sulphate of copper, the same. 5. Sulphurous acid in solution rapidly lost its effect, and was exceedingly irritating to the respiratory organs. 6. Two pounds of impure carbolic acid filled the house for two days with such a disagreeable smell that it was impossible to tell whether the original odor was destroyed or covered up. 7. Two pounds of sulphate of iron in a parchment sack exerted a disinfecting influence for three full days, and when the parchment sack was drawn up it contained only some dirty, odorless fluid. 8. Two pounds of the best chlorinated lime in the parchment sack disinfected the privy for at least nine days.

Lime is probably the oldest of all the disinfectants, but is only of value as a destructive agent,—*i.e.*, as causing a slow oxidation of organic matter. It is notorious that a compost-heap to which lime has been added rots—*i.e.*, oxidizes—much more rapidly than one which has none of the alkaline earth in it. This action of lime is, however, too slow for ordinary purposes: moreover, there are very serious objections to the use of lime as a disinfectant.

The poisonous principles contained in sewage, etc., whatever their nature may be, are probably volatile, and lime, acting as a strong base, sets free large quantities of ammonia in animal matter undergoing decomposition. It may be that volatile poisons, alkaloids, are liberated with the ammonia; but, whether they are or not, it is a well-known physical fact that a volatile substance in escaping carries off with it even non-volatile materials, and facilitates to a still greater degree the escape of principles only less volatile than itself.

Lime is, for the above reasons, not available for use as a disinfectant in cesspools and sewers unless it is added in large quantities day by day from the beginning, so as to keep the collection under its influence, and unless some absorbent is added with it to take up volatile principles. In the ordinary open privies of the country, a shovelful of a mixture of lime and plaster of Paris, or of lime and dry earth, thrown in day by day, will at once tend to prevent odor, and at the same time prepare the contents for use as manure.

When spread upon walls in the form of whitewash, lime may act to some extent as an oxidizer; but probably its chief influence is as an absorbent, which takes up the deleterious emanations. A very striking example or illustration of this action of whitewash occurred some years since in the New York city hospital. A ward which stood isolated from the remainder of the institution had been used for the reception of cases of typhus fever from the shipping of the port. It was finally abandoned and allowed to stand unoccupied, with its windows wide open, for several months. At the end of this time, a gang of men were set to scraping the whitewash off the walls. Of these workmen a majority were seized with the ship-fever, and several died.

CORROSIVE SUBLIMATE.

In 1870, Dr. John Dougall announced that corrosive sublimate, one part in sixty-five hundred would kill spermatozoa, and one part in six thousand, infusoria; the later researches of Koch, Jalan de la Croix, and of Sternberg have more than confirmed this result, and shown that corrosive sublimate is one of the most powerful of known germicides. Micrococci and bacilli in active growth without spores are killed by solutions of one in twenty thousand, while solutions of one in one thousand will rapidly destroy the spores of B. anthracis and B. subtilis. Results contrary to these have, it is true, been obtained by Klein of London, who asserts that a one per cent. solution of the mercuric chloride is no more a germicide than is vinegar; but the strength of the evidence to the contrary is so strong that it seems almost a certainty that there is some error in Klein's experiment. According to the detailed experiment of Koch, the spores of B. anthracis are absolutely incapable of germinating in a proteid solution if as little as one part of corrosive sublimate in three hundred thousand be present. Dr. Sternberg confirms the experiments of Koch, and it would theoretically appear that one part of corrosive sublimate in one hundred thousand is sufficient to destroy germs in a mass of filth, provided that the filth is so situated that the corrosive sublimate will remain in contact with it for some time. It must be remembered, however, that the corrosive sublimate is readily decomposed by the ammonia and other chemical substances in a mass of filth, and it is very doubtful whether in practice it will be found that the mercuric chloride is available for disinfectant purposes on a large scale. Even, however, if its powers be considerably less than they appear to be, it would still remain for many purposes the best of all germicides. A standard solution of one part in a thousand may be used for bedding, which can be soaked in it; for washing the floors and walls of infected apartments; and for disinfecting the hands of surgeons and gynæcologists; after the corrosive sublimate has done its work it should be removed by free washing with pure water. For the destruction of germs in fecal discharges, the solution should have at least the strength of one part in five hundred.

In regard to the use of corrosive sublimate in the treatment of wounds, etc., the reader is referred to treatises on surgery. It is, however, proper here to state that a number of cases of death from the local use of corrosive sublimate, especially in obstetrical and gynæcological use, have been reported. In most of these cases the solution has been at least one part in fifteen hundred, but I have known the use of a vaginal wash, one in ten thousand, to be followed by severe poisoning. It is probably very rarely proper to use continual irrigation of a mucous surface or of a wound with a solution stronger than one in ten thousand; and for a single washing, the solution should not be more than one in two thousand.

POTASSII PERMANGANAS—PERMANGANATE OF POTASSIUM.

U. S. ($KO,Mn_2O_7 — Mn_2O_8K_2$.)

This salt is prepared by heating together ten parts of binoxide of manganese and twelve of potassa. It occurs in slender, prismatic crystals of a dark-purple color, inodorous, of a sweetish, disagreeable taste, and very soluble in water, with which they form a solution varying from a purplish black to a beautiful reddish lilac, according to the strength. When kept dry and not exposed to the atmosphere, the permanganate of potassium is a permanent salt, but whenever in solution it is brought into contact with an organic body it at once gives up its oxygen to the latter, and is converted into potassa and the black oxide of manganese.

The disinfectant power of this salt is beyond question; but at the same time this power is very limited, as the remedy yields up its own oxygen and becomes inert. According to the experiments of Dr. George M. Sternberg (*Med. News*, Jan. 10, 1885), as a germicide the permanganate is very potent, 0.12 per cent. (one part in eight hundred and thirty-three parts) killing the micrococci of pus in two hours. For practical purposes, however, this agent is of very little value as a germicide, because it is at once decomposed by organic matters, and whilst in the laboratory disease-germs may exist almost isolated, in the sick-room they are mixed with a large excess of organic material. Nevertheless the permanganate affords a very elegant disinfectant and germicidal wash for *wounds*, *ulcers*, *abscesses*, etc.; *fetid ozæna*, *otorrhœa*, *leucorrhœa*, etc. In dilute solution its local influence is stimulant and beneficial. When employed in the form of powder it even affects living tissues, acting as a mild caustic, and, as such, may often be applied with advantage to *sloughing ulcers*. As a wash, the strength may vary according to circumstances, from one to twenty grains to the ounce. Internally this salt has been commended in various diseases, in doses of one or two grains. Since it is evident that, even if many grains were taken into the stomach, immediate complete decomposition of them would there occur, the absurdity of this use of the drug needs only to be pointed out. The officinal *Liquor* (*Liquor Potassii Permanganatis*, gr. lxiv to Oj) has no advantages over extemporaneous preparations.

CHLORUM—CHLORINE.

Chlorine gas is officinal only in the form of the *Aqua Chlori*, which is prepared by heating together the black oxide of manganese and muriatic acid, and allowing the chlorine which is generated to pass through water until the latter is saturated. *Chlorine Water* is a greenish-yellow liquid, of a very sharp taste, and having a strong odor of chlorine. When it is desired to liberate chlorine in the air of a room, eighteen parts of finely-ground common salt with fifteen parts of finely-powdered black oxide of manganese should be introduced into a flask; then there should be added forty-five parts of concentrated sulphuric acid and twenty-one of water, previously mixed and *completely cooled*; and, lastly, the flask is to be well shaken. When the evolution of gas ceases, it may be renewed by placing the flask in warm water.* When chlorine is brought into contact with organic substances and moisture, it unites with the hydrogen of the water and liberates nascent oxygen, which rapidly oxidizes and destroys the organic compound. When chlorine comes in contact with sulphuretted hydrogen, it removes its hydrogen and thereby destroys it.

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* Inspired in sufficient amount chlorine gas produces, both in man and the lower animals, narcotism and finally death from paralysis of the respiratory centres (consult *Arch. Exper. Path. und Pharm.*, xiii.).

The germicidal influence of chlorine is very great. Fischer and Proskauer found that dried anthrax spores maintained their integrity for one hour when exposed to the action of a dry chlorine atmosphere containing 44.7 parts of chlorine in 100. When the air and the spores were moist, one hour's exposure to an atmosphere containing four per cent. of chlorine produced complete disinfection. If the exposure was continued for three hours, one per cent. of chlorine was an efficient germicide; and if the spores were exposed for twenty-four hours, the effective proportion of chlorine could be still further reduced. In Dr. Sternberg's experiments (*Rep. Nat. Bd. of Health*, 1880), six hours' exposure of vaccine lymph dried upon ivory points to an atmosphere containing one part of chlorine in two hundred, was sufficient to destroy the infective property of the lymph, whilst the bacteria of putrid urine were destroyed after six hours' exposure to an atmosphere containing one part of chlorine in four hundred.

The result of all our knowledge upon the subject of the disinfectant properties of *chlorine*, *iodine*, and *bromine* is summed up by Dr. Geo. H. Roho (*Med. News*, xlvi. 89) as follows:

1. Chlorine is an efficient disinfectant when present in the proportion of one part in one hundred; provided the air and the objects to be disinfected are in a moist state, and the exposure continues for upwards of one hour.

2. Chlorine, when used in sufficient concentration to act as a trustworthy disinfectant, injures colored fabrics and wearing apparel.

3. Bromine is an efficient disinfectant in the proportion of one part in five hundred; provided the air be in a moist state, and the exposure continues for upwards of three hours.

4. Iodine, in solution, is an efficient disinfectant in the proportion of one part in five hundred; the exposure continuing for two hours.

5. The use of chlorine, and in a greater degree of bromine, requires considerable experience in management; when carelessly handled they may cause inconvenient or even dangerous symptoms in persons using them; for these reasons they are not suitable as disinfectants for popular use.

Internally, chlorine water has been used in various diseases, especially in malignant *typhus*, but at present is very rarely if ever employed. It is stated to be stimulant and tonic to the stomach, and is thought by some to have an especial influence upon the liver. It has been employed in *chronic hepatic affections;* the dose is half a fluidrachm to two fluidrachms in three or four fluidounces of water. Chlorine water is a powerful irritant, capable of producing severe inflammation of the skin or toxic *gastro-enteritis*. Properly diluted, it forms an excellent stimulant, disinfectant, detergent wash for *foul ulcers*, and may also be used as a gargle in *malignant sore throat*.

CALX CHLORATA—CHLORINATED LIME. U. S.

This is a grayish-white substance, occurring in powder or friable lumps, having a hot, acrid, astringent taste, and an odor resembling that of chlorine. It is made by the action of chlorine upon hydrate of calcium or slaked lime, and should contain at least twenty-five per cent. of chlorine. It probably varies in its chemical constitution, but, according to the most recent views, is chiefly composed of the hypochlorite and the chloride of calcium. When exposed to the air it slowly evolves hypochlorous acid, which, being an unstable compound, undergoes spontaneous decomposition, and finally sets free fourteen-fifteenths of its chlorine. When an acid is added to chlorinated lime, the chlorine gas is rapidly evolved. If a specimen of bleaching-powder be very moist, it generally contains an over-proportion of the deliquescent chloride of calcium, and is correspondingly unable to liberate chlorine.

The experiments of Dr. J. R. Duggan (*Medical News*, xlvi. p. 147) indicate that the hypochlorites are among the very best of our practical disinfectants. He found that 0.25 of one per cent. (one part to four hundred) of chlorine as hypochlorites is an effective germicide even when allowed to act for only two minutes; while 0.06 (six parts to ten thousand) will kill the spores of B. anthracis and B. subtilis in two hours.

Bleaching-powder usually contains from twenty-five to forty per cent. of available chlorine. For most purposes, a solution containing one part of this preparation to one hundred of water is strong enough, for this will contain from 0.25 to 0.40 of one per cent. of chlorine as hypochlorite. As is stated above, the smaller of these quantities is sufficient to destroy spores almost instantly. There are very few purposes to which disinfectants are applied that are not fulfilled by this solution of one to one hundred of bleaching-powder. It is not dangerously poisonous, *is said* not to injure clothing, bedding,* etc., and is very cheap, since bleaching-powder is worth only about five cents per pound.† *For the destruction of disease-germs in urine, fecal*

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* This statement seems to me doubtful.

† To fix the value of solutions of the hypochlorites, the following method is, according to Duggan, sufficiently accurate for ordinary purposes. A standard solution of potassium arsenite may be made by diluting seven parts of Fowler's solution with one and a half parts of water. This corresponds to a one-half per cent. solution of available chlorine. To apply the method, a given volume of the hypochlorite solution is measured out, and the arsenite solution added in small quantities. Between each addition the mixture is well stirred, and a drop taken out on a glass rod and tested on a strip of paper saturated with iodide of potassium and starch-paste and dried. As long as any hypochlorite is present, the blue iodide of starch is formed; but when it has all been used up in converting the arsenite into an arseniate, the paper will remain colorless. As each volume of the potassium arsenite solution required for this corresponds to one-half per cent. of available chlorine, the calculation is very simple,—*e. g.*, if one volume of the hypochlorite solution = 4.6 volumes of the arsenite solution, the amount of available chlorine present would correspond to 2.3 per cent. Since the preparations now on the market vary so much in the

discharges, sputum, etc., a saturated solution of bleaching-powder appears to be in all respects the best disinfectant known.

LIQUOR SODÆ CHLORATÆ, U. S.—*Solution of Chlorinated Soda*, or *Labarraque's Solution*, is an officinal preparation, made by triturating chlorinated lime with a solution of the carbonate of sodium. It is a greenish-yellow liquid, having a slight odor of chlorine and a sharp saline taste. It contains, among other substances, hypochlorite of sodium, and possesses the therapeutic and disinfectant properties of the chlorinated compound. Owing to its liquid form, its comparative freedom from odor, and its depositing chloride of sodium on evaporation, it is the most elegant of all the chlorine preparations for use in the sick-room. Properly diluted, Labarraque's solution may be employed for all the therapeutic purposes that chlorine water is used for. The dose is half a fluidrachm to two fluidrachms, in half a tumblerful to a tumblerful of water.

ACIDUM BORICUM—BORIC ACID. U. S.

SODII BORAS, U. S.—*Borax.*—Boric or *Boracic acid* crystallizes in white translucent scales, soluble in about thirty parts of cold water, much more soluble in boiling water, which on cooling precipitates all but about twenty-three grains to the fluidounce. Hot glycerine dissolves and holds upon cooling as much as three drachms to the fluidounce. *Borax* occurs in white, flattened, prismatic crystals, soluble in twelve times their weight of cold water.

The action of boracic acid and its salts upon the animal system is a very feeble one. In experiments made by Dr. E. T. Stewart and myself, enormous doses were required to affect the frog; they depressed the spinal centres and produced progressive loss of voluntary and reflex activity without affecting nerve or muscle. A saturated solution of the quadroborate of sodium brought in direct contact with the heart exercised a very feeble, depressant influence; and when injected in sufficient amount into the jugular vein of the mammal lowered the arterial pressure. Cyon (*Hoffmann und Schwalbe's Jahresb.*, 1879, 301) has found that daily doses of three drachms of borax increase the appetite and digestion in dogs without causing other effect, unless it be gain in weight. Max Grüber* (*Ibid.*, p. 351), in a series of experiments, found that the elimination of urea and of

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amount of chlorine they contain, this test should always be used to determine their value, and the amount of dilution required.

* A very curious effect is said, by Prof. Schiff (*Rev. Med. de Suisse Rom.*, 1881, 244) to be produced by the local application of boracic acid to nerves; the part affected is affirmed to lose its power of originating but not of transmitting impulses, so that if the galvanic current be applied to the part of the nerve which has been exposed to the drug no muscular contractions result, but if the poles be placed above this part, the distal muscles respond at once.

water by the kidneys is increased by large doses of borax. Mododewkow is said (*St. Louis Clin. Rec.*, Sept. 1881) to have had two cases of fatal poisoning with boracic acid; in the one case a lumbar abscess, in the other a pleuritic cavity, was washed out with a five per cent. solution of the acid, much of which remained. The symptoms were nausea, incessant vomiting, hiccough, erythematous eruption, fall of temperature, and collapse, the mind remaining clear. In a not fatal case (*Med. News*, xl. 704) the symptoms were erythema, with rapid, feeble pulse. Dr. R. Hogner reports (*Schmidt's Jahrb.*, Bd. ccii. 238) two cases in which washing out of a dilated stomach with a two and a half per cent. solution of boracic acid was followed by erythematous eruption, headache, great general distress and weakness, disturbance of respiration, coma, involuntary discharges, ecchymoses on the skin, and death.*

In the experiments of Dr. Walb (*Centralb. Klin. Medicin*, 1882, iii. 529), two per cent. solution of borax distinctly checked the putrefaction of solution of fibrin; a five per cent. solution kept the solution fresh for nineteen days. Fresh muscle-fibres from oxen were kept fresh many days by a one per cent. solution. In the elaborate experiments of Dr. Sternberg it was found that boracic acid and the biborate of sodium. are inefficient as germ-destroyers, but have considerable antiseptic power (*Amer. Journ. Med. Sci.*, lxxxiv. 321).

Recently boracic acid has attracted attention as a disinfectant, or rather antiseptic, and its power seems to be undisputable, although further experiments are necessary to settle its exact value. In 1874, Dumas and Schnatzles announced that borax is poisonous to the lower forms of life (*Pharm. Journ.*, April, 1874); in Bucholz's experiments, 0.75 per cent. of boracic acid was found sufficient to prevent the development of bacteria (*Arch. Exper. Path. u. Pharm.*, Bd. iv.). The acid has been used to a considerable extent in antiseptic surgery, and it is affirmed to be free from irritating properties, and of great practical value in the treatment of fresh wounds, foul ulcers, abscesses, old burns, etc. (see especially Dr. M. Greene, *Boston Med. and Surg. Journ.*, ciii. 209). *A lint* may be made by saturating ordinary patent lint with a saturated boiling solution of boracic acid; wounds dressed in a dry manner with this are stated to heal as rapidly as when a complicated antisepsis is employed. Dr. Greene prepares an ointment by melting one part each of spermaceti and white wax with six parts of vaseline, and adding, whilst hot, two to four parts of a saturated glycerite of boracic acid. In the form of lotion, the remedy has been used with great advantage in *phlegmonous erysipelas* (see *London Lancet*, May, 1873; May, 1876; also, Prof. F. L. Lebovicz, *Gaz. Hebdom. de Méd.*, xxi., 1884, p. 624). There can be doubt of the value of boracic acid and borax as a local application in *aphthous ulceration*, *diphtheria*, and other *inflammations* of the *mouth*, in which crystals of the sodium salt may be allowed slowly to dissolve in the mouth; whether, as affirmed by Dr. William Greene and by Dr. F. P. Atkinson (*Lond. Practitioner*, xxiv. 254), boracic acid is useful in *septicæmia*, *puerperal fever*, *erysipelas*, etc., is more problematical.* The statements of Prof. Rosenthal (*Allegm. Wien. Med. Wochens.*, Jan. 1884), that boracic acid is efficient in *ammoniacal* urine and *cystitis*, acidifying the urine and checking the fermentation, have been confirmed (see *Lond. Lancet*, ii., 1884, 133). The acid may be given in doses of ten grains three to six times a day; the salt, twenty grains to a drachm; in each case administered in diluted watery solution. As a disinfectant and soothing eye-wash its solution is much used by oculists in conjunctival inflammation and irritation. The strength may vary from five grains to the ounce up to saturation. In the *cystitis* of *spinal diseases* I have secured great relief by washing out the bladder with a few ounces of a saturated solution of boracic acid after the use of the catheter.

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* There is no reason for believing that boric acid had anything to do with the symptoms in the alleged case of poisoning reported in *Med. News*, xliii. p. 199.

ACIDUM SULPHUROSUM—SULPHUROUS ACID.

Sulphurous acid and its salts are most efficient in destroying the low forms of life which are connected with putrefaction and fermentation, and for this reason are excellent preservatives of organic matters.

Sulphurous acid and its salts are among the oldest of disinfectants, having been used as long ago as 1771; but recent experimental evidence seems to indicate that they have not the great superiority which has been attributed to them. According to the experiments of Sternberg one volume of sulphurous acid gas in one hundred volumes of air is sufficient to disinfect dry vaccine matter. As these experiments are in accord with older observations they may be considered as correct.

According to Wernitz, the action of pepsine, of ptyaline, of invertine, and of diastase is prevented by the presence of an aqueous solution of SO_2 of 1 : 1317 to 1 : 8600 (by weight); while the action of myrosine and of emulsine is neutralized by 1 : 21,000.

According to Wernick, strips of woollen or cotton goods saturated with putrefactive matter are disinfected by exposure of from four or six hours to an atmosphere containing four per cent. of sulphurous acid gas. The very elaborate experiments of Koch, of Wolffhügel, and of Sternberg have shown, however, that when the infectious material contains spores sulphur dioxide is of very little value. Wolffhügel concludes that it should be abandoned as a disinfectant; nevertheless, as probably but few of the contagions are in the condition of spores, sulphurous acid is probably, when sufficiently concentrated, an effective disinfectant, if applied for a sufficient length of time. It has been proven by the experiments of Sternberg that the gas acts much more freely and powerfully when the air is loaded with moisture. Fumigation of an apartment with sulphurous acid gas should never be allowed to take the place of cleanliness and thorough disinfection of the walls and of all articles of furniture. Whether after all this is done the fumigation does any good—whether in practice it is of any real value, remains doubtful. It is perfectly sure that it is of no service unless the air of the room be made to contain at least five volumes per thousand of the gas, and this for a period of from four to six hours. The following method is the one generally employed.

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* M. Cyon commends most highly the use of borax in daily doses of eighty to ninety grains as a prophylactic against *cholera*, and affirms that during the epidemic in Italy during 1864–65, none of the villagers employed in the borax works were affected, whilst in a village in close proximity one-third of the inhabitants died. He believes that the drug kills the germs in the alimentary canal (*Comp.-Rend. Acad. Sci.*, xcix. 149).

Take a large iron pot or caldron, put in a little stand, such as the cheap tripod used by chemists, place on this an iron plate containing flowers of sulphur thoroughly wet with alcohol or (probably better still) with turpentine; underneath the plate set a tin alcohol lamp; then put the whole on bricks in the middle of the room. Light the lamp underneath the dish, and if the sulphur does not take fire previously, when it begins actively to melt, ignite it. Leave the room at once, closing the door. The room should be as tight as possible, the chimney-places, ventilators, windows, and doors of exit being closed, whilst all the drawers of furniture and the doors of closets are widely opened.

Sulphurous acid may be used in a saturated solution for the purpose of destroying disease-germs in the excretions of the sick;* its action upon vegetable colors of course completely unfits it for many uses. The sulphites and the bisulphites are largely employed to arrest or control fermentation in various processes in the arts.

ACIDUM CARBOLICUM—CARBOLIC ACID. U. S.

Phenic Acid, or *Phenylic Alcohol*, is a substance obtained from coal-tar by distilling at a temperature of between 300° and 400° F., adding to the distillate a hot concentrated solution of potassa, and after this water, separating the light oily matters which rise to the top, and adding muriatic acid to the heavy alkaline bottom layer, when impure carbolic acid separates. This impure carbolic acid (*Acidum Carbolicum Crudum*, U. S.) is of a dark color, and contains several congeneric bodies, especially xylic and cresylic acids. For disinfectant purposes these appear to be at least of equal value with the carbolic acid, and therefore the crude product of the above-detailed process is very largely used. Carbolic acid is separated from its allies and obtained in a pure state with some difficulty, by a process too complex to be discussed here. When finally procured, it occurs at ordinary temperatures in minute, colorless, transparent plates, or long rhomboidal needles, often fused into a mass, having a hot, corrosive, peculiar taste and a peculiar odor, resembling but entirely different from that of creasote. If, on exposure to the air, phenic acid becomes brown, it contains impurities. When opportunity is afforded, solid carbolic acid absorbs water from the atmosphere and melts into an oily-looking colorless liquid. It is inflammable, neutral to test-paper, but combines with bases; soluble in about twenty parts of water, very soluble in alcohol, acetic acid, ether, glycerine, and the volatile and fixed oils. Nitric acid converts it into picric acid.

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* For a very interesting account, by Dr. J. Hjaltelin, of the strangling of a smallpox epidemic in Iceland, see *British Medical Journal*, 1871, vol. ii. p. 519. I cannot help believing that the strict isolation and quarantining of the sick had far more to do with arresting the spread of the disease than had the sulphurous acid employed.

CREASOTUM, U. S.—*Creasote* is a substance closely allied to carbolic acid, and is prepared from wood-tar, by a process similar to that by which the latter is obtained from coal-tar. It resembles closely carbolic acid solutions, but may at once be distinguished by its odor, which is much more smoky. Moreover, if a splinter of pine be dipped into carbolic acid, and then into muriatic acid, the wood, after the lapse of half an hour, assumes a distinct blue color. This does not occur with creasote. Again, carbolic acid does, and creasote does not, coagulate collodion; and by the action of nitric acid creasote is converted into oxalic acid, resinous matter, and but a small proportion of picric acid. Creasote is at present a rare drug, the material which is usually sold under its name in the drug-stores being really a solution of carbolic acid. In their therapeutic value the two substances are probably about equal.* Five cases of poisoning are on record: Müller (*Würtemb. Correspondenz Blatt*, 1869), T. Stevenson (*Guy's Hosp. Rep.*, xx., 1875, 144), Pürckhauer (*Friedreich's Blätter für Gericht. Med.*, 1883, 430), F. Grinell (*Med. News*, xl. 345), Manouvriez (*Soc. Méd. Légale de France*, vii. 108). The symptoms are like those of carbolic acid poisoning,—*i.e.*, unconsciousness, collapse, stertorous breathing, and great cardiac depression.

PHYSIOLOGICAL ACTION.—Carbolic acid is exceedingly poisonous to all forms of life, from the lowest to the highest. Much of its employment in medicine depends upon its action on infusoria and fungi; and yet its direct internal and external use in human medicine is quite large. Its physiological action is therefore to be viewed from two distinct stand-points: first, its influence upon the higher animals and man; second, its action on the lowest animal and vegetable forms.

Upon mammals, if not upon all vertebrates, carbolic acid acts as it does upon man. According to Dr. Isidor Neumann (*Archiv für Dermatol. und Syphilog.*, Jahrgang i., 1869, p. 425), to Dr. Ernest Labée (*Archives Gén.*, 6e sér., t. xviii. p. 451, 1871), and to Salkowski (*Pflüger's Archiv*, Bd. v.,

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* *Creosol* appears to be the basis of pure creasote; from it is easily prepared *creosotinic acid*. This substance has been found by E. Buss (*Berlin. Klin. Wochens.*, 1876, p. 445) to have active antipyretic and other therapeutic properties.

1872), when a poisonous dose is given to a frog there is produced a paralytic condition which usually affects first the hind legs,* but eventually spreads to the front ones and involves all parts of the body. After a time there are developed tetanic convulsions, which are apparently reflex in their nature, and are said to be excited by external stimuli or irritations.

Carbolic acid acts upon mammals in very much the same way as upon the batrachian. According to W. Kempster (*Amer. Jour. Med. Sci.*, July, 1868), in the mouse and rat it causes intense muscular weakness, followed by violent convulsions and stupor. In the rabbit (Neumann, Salkowski), phenylic alcohol produces muscular weakness, often accompanied by tremblings and restlessness, at last giving place to violent convulsions. Before these have fairly set in, the animal is generally unable to stand; and during them he lies on his side, kicking into mid-air. Early in the poisoning the respiration is very much affected; and the death, which usually occurs in the midst of convulsions, appears to be owing to a disturbance of the respiration, since in acute cases the heart is found beating continuously immediately after death. According to the researches of Dr. Jules Lemaire (*De l'Acide Phénique*, 2e éd., Paris, 1865), in the dog symptoms very similar to those detailed above are caused by lethal doses of the drug; and Husemann (*Schmidt's Jahrb.*, Bd. clv. p. 274) states that in mammals and in birds the characteristic phenomena of carbolic acid poisoning are clonic convulsions, sinking of the temperature, diminution of sensibility, dyspnœa, free salivation and secretion of tears, keratitis and conjunctivitis. According to the latter authority, albuminuria and hæmaturia are occasional phenomena. Upon man carbolic acid acts as upon other mammals. Reserving the details for the section on Toxicology, it is sufficient for our present purpose to state that the prominent symptoms induced by lethal doses are disturbance of respiration, coma, muscular weakness, and, in some cases, convulsions. A closer investigation of the action of large doses of carbolic acid is best made by studying the effects upon the different systems *seriatim*.

Nervous System.—Upon the cerebrum phenylic alcohol appears to exert a direct influence, which, although not very intense in the lower animals, in the higher species, and especially in man, results in the early production of stupor.

These convulsions are not peripheral, since they do not occur in a limb whose connection with the spine has been severed by division of the nerve, and do take place in a leg which has been protected against the local action of the poison by tying the artery (Salkowski, Labée). They are, therefore, either cerebral or spinal. Although there is a distinct conflict of evidence, it seems to me established that they are of spinal origin. Labée and Jno. R. Haynes failed to get them after section of the cord, but in the far more numerous experiments, upon frogs and mammals, of Salkowski, of Berb and Jogel (*Gaz. Méd.*, 1872), of J. S. Stone (*Philad. Med. Times*, ix.), and of T. Gies (*Arch. f. Exper. Path. und Therap.*, xii. 401), convulsions occurred after destruction of the medulla, section of the cord, and other operative procedures separating the brain from the lower nervous system. The failures of the first-named experiments are explainable by the facts that the paralyzing influences of carbolic acid are usually first manifested upon the hind legs, and that very large doses of the acid were employed. The spinal convulsions are accompanied by increased reflex activity, which is lost as the paralytic state is reached, so that carbolic acid appears first to stimulate and then depress the spinal centres. Stone asserts that the stimulation is preceded by a primary depression, due to stimulation of Setschenow's inhibitory centre in the medulla.

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* According to Lemaire, when a frog is allowed to swim in water impregnated with carbolic acid, the front legs are the first affected.

In carbolic acid poisoning the nerves and muscles are not distinctly paralyzed, galvanic stimulation of a nerve after death eliciting vigorous response in the tributary muscle (Salkowski, *loc. cit.*, 338; Hoppe-Seyler, *loc. cit.*, 476); but the very careful experiments of Gies (*loc. cit.*, p. 413) have proven that such muscles are less sensitive and more easily exhausted than in the unpoisoned animal.

Circulation.—The action of carbolic acid upon the heart is not a very marked one, but there can be little doubt that in sufficient amount the drug depresses the viscus. After death from acute poisoning the heart is usually found to be beating regularly (Salkowski), but in some cases of slow poisoning the death has seemed to be ultimately caused by cardiac diastolic arrest. In Hoppe-Seyler's manometrical studies (*Pflüger's Archiv*, 1872, Bd. v. 475) the arterial pressure was not affected until convulsions came on, when it rose largely, as a result of the general muscular contraction. It afterwards fell very decidedly and permanently. Reduction of the arterial pressure has been shown by Gies to be the characteristic effect of the carbolic acid: in his experiments moderate doses of the acid failed to affect the pressure after section of the cord, whilst neither asphyxia nor stimulation of a sensitive nerve elevated the lowered pressure, although the heart was beating forcibly,—facts that demonstrate that carbolic acid *paralyzes the vaso-motor centre* in the medulla before it markedly affects the heart.

Respiration.—According to Salkowski (*loc. cit.*, p. 344), Labée, and other authorities, in the first stages of carbolic acid poisoning the respiration is remarkably increased in frequency. This acceleration Salkowski believes to be due partly to a stimulant action upon the peripheral vagi, and partly to a similar influence upon the respiratory centres. He states that the respirations are very shallow, and that the diaphragm scarcely participates at all in them, but that if the cervical vagi be cut they become much slower, deep, and regular. On the other hand, if carbolic acid be given to an animal suffering from section of the pneumogastrics, the slow breathing is very much accelerated. From the former of these facts the German investigator draws the conclusion that the accelerated breathing produced by phenylic alcohol is in part due to a stimulation of the peripheral vagi, and from the latter fact that it partly arises from a similar action upon the respiratory centres.

Temperature.—The effects of carbolic acid upon the temperature in the normal animal have not, that I am aware of, been studied, but Emil Erb (*Schmidt's Jahrbücher*, Bd. clxiv. p. 148) has found that in mild putrid poisoning in animals it diminishes greatly the fever-heat; when the poisoning was more severe the acid had no influence.

In sufficient concentration carbolic acid seems to be poisonous to all forms of protoplasm. Dr. T. M. Prudden (*Am. Journ. Med. Sci.*, lxxxi. 82) finds that in strong solution it paralyzes, in weak solution depresses, the movements of the batrachian white blood-corpuscles and ciliated cells, and Labée has determined that outside of the body it materially affects the blood of mammals. Both Labée and Hoppe-Seyler (*Pflüger's Archiv*, v. 476), however, affirm that the blood of higher animals poisoned by carbolic acid presents nothing abnormal, so that the symptoms it produces must be the result of a direct influence upon the various tissues.

Post-mortem examinations of animals killed by carbolic acid have yielded varying results. In Lemaire's investigation, nothing abnormal was found except intense injection of the alimentary mucous membrane, a pseudomembranous and purulent inflammation of the bronchial tubes, with a disseminated lobular pneumonia or else congestion of the lungs and of the nerve-centres. Prof. Bruckmüller, in Neumann's investigation (*loc. cit.*, p. 429), found the cells of the liver and kidneys in a state of fatty degeneration. This process, which seemingly was the counterpart of the changes in phosphorus-poisoning, was always more advanced in the kidneys than in the liver. Dr. Neumann states that it was found in a number of autopsies, and that it is a constant phenomenon; but Salkowski (*loc. cit.*, p. 273) was unable to find it in a number of examinations. In man, the post-mortem appearances are very much the same as in animals. If the acid has been ingested in a concentrated form, white, hardened spots are found upon the mucous membrane of the mouth, œsophagus, stomach, and even intestines. They are, of course, due to the local action of the poison, and are sometimes blackish in the centre, or even blackish throughout, and very generally are surrounded by a red inflammatory zone. The liver, spleen, kidneys, and indeed all the organs, are found filled with dark, imperfectly-coagulated blood, such as is habitually found after death from asphyxia. According to Husemann, the fatty degeneration of the liver and kidneys is not either in man or in animals a constant or characteristic phenomenon of carbolic acid poisoning. Reuder found the renal epithelium degenerated in a man who had been fatally poisoned by the drug (*Journal de Pharm. et de Chimie*, p. 456, Dec. 1871).

As the internal use of carbolic acid in such diseases as gangrene of the lungs is so closely connected with the question of its chemical history in the system and its elimination from the body, the latter is of very great interest. Since carbolic acid coagulates albumen, its absorption unchanged into the blood would seem a matter of doubt: yet in some form or other it certainly is absorbed, as is proven by the history of its elimination and by its having been found in the blood (Hoppe-Seyler, *Pflüger's Archiv*, Bd. v. p. 479). In exactly what form it circulates in the blood is not known; but most probably it is as an alkaline carbolate. Lemaire (*loc. cit.*, p. 77) states that it may be found in the breath of poisoned animals; but Hoffmann asserts that it is burnt up in the system, because he failed to detect it in any of the secretions. In this conclusion he is, however, certainly in error; for it has been distinctly proven that carbolic acid is rapidly eliminated from the system. It has been detected in the urine by Almén (*Zeitschrift f. Analyt. Chimie*, Bd. x. Heft vii.), by Patrouillard (*Journal de Pharmacie et de Chimie*, Dec. 1871, p. 459), by Salkowski (*Pflüger's Archiv*, Bd. v.), by Hoppe-Seyler (*loc. cit.*), by Waldenström (*Zeitschrift des Allgemein. Apothek.-Vereines*, Jan. 10, 1872), and by Hauxmann (*Ibid.*); and Hoppe-Seyler (*loc. cit.*, p. 480) has detected it in the saliva. It is probably eliminated in all the secretions. The researches of Baumann (*Zeitschr. f. Physiol. Chem.*, 1878, 350), which have been substantially confirmed, show that the carbolic acid is changed into a peculiar sulphocarbolic acid, a sort of ether-sulph-acid, having the formula $C_6H_5O.SO_2.OH$, which finally unites with potash and is eliminated as a sulphocarbolate; when large quantities of the acid are administered, some of it escapes unchanged, for in a fatal case of poisoning, Patrouillard (*Zeitschr. des Allgemein. Apothek.-Vereines*, p. 460) obtained an oily fluid, believed to be pure carbolic acid, by shaking the urine with ether, allowing the mixed fluids to separate, and removing the ethereal layer and evaporating.

Although, as stated, carbolic acid is to some extent eliminated from the system, a portion of it is burnt up in the body. The black coloring-matter of the characteristic urine of carbolic acid poisoning is in all probability an educt from carbolic acid, formed by its partial oxidation. Hauxmann has proved that it is not altered hæmatin or any fixed coloring principle, by finding that the urine is cleared up by heating after the addition of an acid; and his conclusion is corroborated by the observation of Dr. Stevenson, of Guy's Hospital (*Brit. Med. Journ.*, April, 1870), who found that the black urine does not contain more than a normal proportion of iron. When carbolic acid is oxidized outside of the body, as by the action of the permanganate of potassium, oxalic acid is formed; and Salkowski has found that when phenic acid is given to animals oxalic acid appears in the urine. Other observers have, however, failed to find these oxalates. Fr. Schaffer (*Journ. f. Prakt. Chem.*, xviii. p. 282), A. Uerbach (*Virchow's Archiv*, lxxvii. 226), and E. Baumann and C. Preusse (*Zeitschr. f. Physiol. Chem.*, iii. 156) found that the phenol was at least in part oxidized into *hydro-*

chinion, and partly into a greenish-black substance upon which the colorng of the urine seems to depend. The recent researches of L. Brieger (*Zeitschr. f. Klin. Med.*, 1881, ii. 25) seem to prove that when carbolic acid is taken in not too large quantities a portion of it unites with sulphuric acid, and a portion of it is converted into various colored oxidation products, some of which are very poisonous. According to the experiments of W. Kochs, this change occurs in the large abdominal glandular viscera (*Arch. f. Physiol.*, xx. 64, xxiii.). Schmiedeberg has recently come to the conclusion that no phenol is oxidized in the body, but that it is all eliminated in combination with sulphuric acid, or to a less extent with glyco-uronic acid (*Arch. Exper. Path. u. Therap.*, xiv. 288). The evidence is, however, too strong against this view, and the true conclusion seems to be that when carbolic acid is taken *in great excess it is in part eliminated as carbolic acid*, and that the remainder of it (the whole of it when taken in moderate amount) *in part* escapes in combination *with an alkali as sulpho-carbolic and glyco-uronic acids and is in part oxidized in the system.*

Städeler (*Ann. d. Chem. und Pharm.*, Bd. lxxvii. p. 17) discovered that when sulphuric acid was freely added to cow's urine the latter yielded upon distillation carbolic acid, and concluded therefrom that normal urine contains carbolic acid. He has been corroborated by Buliginsky (*Hoppe-Seyler's Med.-Chem. Untersuch.*, p. 234) and by Hoppe-Seyler (*Pflüger's Archiv*, 1872, Bd. v. p. 470), and phenol is certainly a constituent not only of the urine of cattle, but also of that of men, dogs, horses, and probably other animals. Baumann has succeeded in producing carbolic acid out of fibrin by a protracted digestion with the pancreatic glandular substance, and Neucki and Brieger have found that it is constantly present in normal human fæces. It is probable, as asserted by Salkowski, that the acid is formed in the organism as a late product of the pancreatic digestion. Its elimination by the urine is enormously increased in ileus (one-hundredfold, Salkowski), and diminished in anæmia, phthisis, scorbutus, scrofula, and cancer (Brieger, *Med. Centralb.*, 1878, p. 545). Hoppe-Seyler's theory that the acid does not pre-exist in the urine, but is formed out of indican during the processes employed for procuring it, is not tenable. It appears to be formed from the albuminous substances, tyrosin being an intermediate product, since Brieger has found that the taking of large doses of tyrosin is followed, not by elimination of tyrosin, but by a great increase of the urinary phenol. In this connection it is interesting to note that Christiani has found in the urine of chickens fed upon vegetable diet no phenol, but a notable amount when a flesh diet was allowed (*Zeitschr. f. Physiol. Chem.*, ii.). In a series of experiments Dr. I. Munk obtained three grammes as the average excretion of twenty-four hours from a horse (*Arch. f. Thierheilkunde*, viii. 104).

The local action of carbolic acid is a very decided one. When applied to the skin, it produces at once a burning pain, and in a few minutes a peculiar white spot. If the acid be removed, the pain continues for some minutes, and the white color changes to a dark or red stain, which gradually fades away as the skin desquamates. On a prolonged application, carbolic acid does not blister, but causes the formation of an eschar. A curious local action of carbolic acid, to which attention was drawn almost simultaneously by Dr. Erasmus Wilson (*Journal of Cutaneous Medicine*, June, 1870) and by Dr. J. H. Bill, U.S.A. (*American Journal of the Medical Sciences*, Oct. 1870), is due to the property which it has when applied in concentrated form of causing very great local anæsthesia. The complete loss of feeling is not confined to the tissue killed by the drug, but extends some little distance inwards.

THERAPEUTICS.—In the doses in which it is usually given, carbolic acid exerts no perceptible effect upon the system. It has been used to a considerable extent in zymotic diseases for the purpose of destroying the poison in the blood. Even, however, if such poison be micrococci or bacteria there is no reason for believing that these are more sensitive to the action of the drug than is the human organism, and clinical experience with the acid in these diseases has certainly demonstrated its uselessness. The study of its physiological action has failed to show the possession of any property which should render the medicine valuable in constitutional diseases. Our physiological knowledge conforms with clinical experience in showing that carbolic acid is of no value in constitutional diseases, and it is employed directly in medicine only for its local effects.

Internally it is of value in *nervous vomiting*, especially when there is an irritability of the gastric nerves. One or two drops of it, or of creasote, may be given in emulsion every three or four hours in such cases. The good which it achieves is probably dependent upon its local anæsthetic properties. In *gangrene of the lung*, the internal administration of carbolic acid, combined with the use of a weak solution (ten drops to the ounce) by atomization, is sometimes of service.

Prof. M. H. Desplats has used carbolic acid as an antipyretic with asserted good results, but the practice seems to me a very doubtful one. He gives from fifteen to thirty grains of the acid by the rectum, and states that he has administered as much as three drachms a day without injury (*Gaz. Hebd.*, 1880, xvii. 628).

Its external use is much more important than its internal employment; but it belongs to the domain of the surgeon rather than of the physician, and I shall only discuss it briefly.* As a *caustic*, carbolic acid is not available when large masses of tissue are to be destroyed, but it may often be employed with advantage against *condylomata* and similar growths. Even in such cases, to be efficient, it must be in the most concentrated form. In *diphtheria*, *ulcerated sore throat*, and *aphthous stomatitis*, its concentrated solution in glycerine may be carefully applied, by means of a camel's-hair brush or a mop, as a mild caustic scarcely capable of destroying sound tissue. In various forms of *indolent ulcer*, in *ill-conditioned wounds*, carbolic acid affords a very useful stimulant application; in "*burns*," properly diluted with oil (gtt. x to f℥i), it is one of the very best remedies that can be used, relieving pain by its anæsthetic properties and at the same time lessening suppuration and facilitating cicatrization.

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* Perhaps it is proper here to call attention to the experiments of Dr. L. A. Stimson (*Am. J. Med. Sci.*, lxxix. 83), which seem to show that the carbolic acid spray, as used by Lister, has no effect upon floating germs.

As a local anæsthetic, carbolic acid has not been used so widely as it seems to deserve. Dr. Bill (*loc. cit.*) has employed it in a number of cases of minor operations, always with the result of preventing or greatly mitigating pain. His plan in opening a felon is to soak the fingers for fifteen minutes in warm water containing three per cent. of the acid, and then to draw a brush dipped in the concentrated acid along the line of the incision. Sometimes, when a deep incision is necessary, a sensitive part is reached. Under these circumstances he is accustomed to brush out the wound anew with the anæsthetic. In operations requiring much cutting, this method is not available; but whenever only the skin is to be divided, as in opening *abscesses*, it appears to be very successful.

So far as I know, the first to suggest and employ *deep injections* of carbolic acid as a means of combating *deep-seated inflammations* was Dr. J. A. Eames (*British Med. Journ.*, May, 1873); but the method has been especially studied by Prof. C. Hueter (*Deutsch. Zeitsch. f. Chir.*, iv. 1874; *Schmidt's Jahrbücher*, Bd. clxiv. p. 144). He employs a two per cent. solution, a weaker one not being efficient, and a stronger one endangering the coagulation of the blood and of the exudation in the inflamed tissue. Of this solution he uses at one time never more than half a drachm, and generally less than this.* After anæsthetizing the skin by the local application of carbolic acid, he introduces the hollow needle into the centre of the inflammation obliquely, so as to diminish as far as possible the chances of the introduction of air. To avoid the danger of throwing the acid directly into the circulation, the needle is not connected with the syringe until it is seen that no blood comes out through it. If the extent of inflamed tissue be large, several injections are practiced at one time; in acute cases they are usually repeated twice a day, in chronic cases every day, or every other day. Dr. Hueter has made about a thousand of these "parenchymatous injections," and only ten times has any inflammation been excited by them. The pain is usually very slight, and the relief apparent in one or two days at most. In *chronic synovitis*, the drug is thrown into the joint once in two or three days, and the method has been practiced by Dr. Hueter with asserted extraordinary success in *glandular swellings and inflammations*, *phlegmons*, of all grades and characters, *erysipelas*, *poisoned wounds*, *inflamed bursæ*, *hydrocele*, and even in bone-disease.

The practice has been followed with satisfaction by Dr. Aufrecht in *erysipelas* (*Centralbl. Med. Wissen.*, 1874, p. 129), by Senator (*Berlin. Klin.*

Wochens., 1876, p. 69), Mader (*Centralbl. für Chir.*, 1877, p. 376), and Kunze in acute and subacute *rheumatism* (*Centralbl. Med. Wissen.*, 1874, p. 479), by Hagen in several diverse inflammations (*Schmidt's Jahrb.*, Bd. clxiv. p. 146), and by I. Schmidt in chronic *synovitis* (*Centralbl. Chir.*, 1876, p. 552). Dr. Hagen has even used these injections with very excellent results in three cases of severe *angina* which he believed threatened diphtheria, throwing the remedy into the neighborhood of the second tracheal cartilage (*Ringknorpel*). Dr. Moses K. Taylor (*Amer. Jour. Med. Sci.*, April, 1882) has used injections in one hundred and fifty cases of buboes and otherwise enlarged glands with uniform success. He throws into the inflamed part about twenty minims of an eight-grain solution of the acid, previously chilling the surface with an ether spray. The total evidence seems to show that this method of treatment is both safe and effective.

TOXICOLOGY.—The number of fatal cases of carbolic acid poisoning now on record is quite large, and the list is constantly growing.* The symptoms although varying within certain limits, are, on the whole, quite uniform. They almost always appear in a very short time after the ingestion of the poison. Sometimes the rapidity of the fatal result almost equals that of prussic acid poisoning. Thus, Dr. Taylor, U.S.N. (*Philadelphia Medical Times*, vol. ii. p. 284) records a case in which about an ounce is supposed to have been ingested, and in which the man fell unconscious within ten seconds after taking the fatal draught, two minutes afterwards was totally unconscious, pulseless, with irregular distant gasping respirations, and in less than a minute later was dead, apparently from cardiac paralysis, since the impulse of the heart was entirely lost before the cessation of respiration. Generally some minutes elapse before the symptoms develop themselves: nausea, cold sweats,† stupor deepening rapidly into insensibility and collapse, are the most frequent phenomena. During the period of insensibility, complete abolition of reflex movements and anæsthesia of the mucous membranes have sometimes been noted (case, *Journ. de Pharm. et de Chim.*, Dec. 1871): indeed, it is scarcely doubtful that in all cases both sensibility and reflex movements are profoundly affected. Convulsions are only exceptionally present. The symptoms of collapse are usually well developed, and the pulse is generally feeble and very frequent, but has been noted as being reduced to from forty to fifty per minute (case, *Med. Times and Gaz.*, April, 1871). Hæmoglobinuria has been noted. Dyspnœa is often extreme; the respirations may be stertorous, are usually very rapid, and, in the advanced stages, shallow. In very rapid cases they are irregular and suspended at intervals. Total temporary amaurosis, with contraction of the pupil, has been noted (case, *Berlin. Klin. Wochensch.*, xix. 748). Death may occur in a very few minutes; but usually the patient lives from one to ten hours, and life has been protracted for sixty hours (case, *Sydenham Year-Book*, p. 446, 1871–72; amount taken, one and a half ounces of the commercial acid). In some cases a great amendment has occurred and consciousness been restored, but after some hours rather sudden fatal collapse has come on (case, *Brit. Med. Journ.*, Feb. 1861). The minimum fatal dose of carbolic acid is not known; but half an ounce has several times caused death (*Med. Times and Gazette*, 1870, ii., p. 474; *Philad. Med. and Surg. Rep.*, Jan. 1870; *Lancet*, 1878, ii., p. 510), and a little over a drachm is reported to have killed a man sixty-four years old (*London Lancet*, 1869, i.); in a case of puerperal metro-peritonitis fifty drops contributed towards the fatal result (Dr. A. D. L. Napier, *Trans. Med.-Chir. Soc. Edinb.*, ii. 75).

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* References to one hundred and sixty-nine cases of carbolic acid poisoning have been collected by H. Kobert (*Schmidt's Jahrb.*, cxciv. 229).

† The excessive sweating sometimes seen in carbolic acid poisoning Th. Gies believes to be of central origin, since in a poisoned cat with one sciatic nerve cut, no sweat came from the injured part.

The free external use of carbolic acid is by no means devoid of danger: Dr. Falckson, after two hours' exposure to carbolic acid spray, recovered from his urine thirty grains of carbolic acid (*Arch. Klin. Chirurg.*, xxvi. 204), and he describes a marasmus or chronic poisoning resulting from the surgical use of the remedy. The symptoms are said to be headache, loss of appetite, bronchial irritation, which finally may become very severe, severe pains in the region of the kidney, recurring vomiting, pruritus, or various paræsthesiæ, and loss of power in the legs. (See also paper by Dr. Wallace (*Brit. Med. Journ.*, April, 1870).

There have been numerous cases of acute poisoning from the external use of carbolic acid. A single vaginal injection has produced very severe constitutional results (*Schmidt's Jahrb.*, Bd. cci. 129). Prof. R. Köhler reports (*Schmidt's Jahrb.*, Bd. clv. p. 276) the cases of two journeymen joiners, suffering from scabies, who applied externally each about a half-ounce of carbolic acid, in watery solution. One of them was found dead. His fellow, who suffered from unconsciousness and drunken delirium ending in unquiet sleep, after his recovery, stated that directly after rubbing himself with the solution he had giddiness, that seven or eight minutes later his companion complained of burning, but that of what took place after this he knew nothing.[*] It is scarcely necessary to refer in detail to cases in which serious results have followed the surgical use of carbolic acid.[†] In vol. ii., 1870, of the *Medical Times and Gazette* is narrated a curious case of fatal poisoning from inflammation of the external parts and of the rectum, produced in a child by its sitting upon a block on which some of the acid had been thrown. A serious result which has been known to follow the application of phenol to a slight wound of the finger is gangrene of the whole member (*L'Abeille Méd.*, Dec. 11, 1871). It is affirmed with somewhat doubtful truth that the absorption in these cases is through the surrounding skin, rather than from the wound, and that if contact of the carbolic acid dressing with the skin be prevented by a coating of gutta-percha upon the latter, all danger of poisoning is averted (*Med. Times and Gaz.*, ii., 1878, p. 461).

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[*] For other fatal cases, consult *Bulletin Thérap.*, t. lxxv. p. 285.

[†] Consult *British Medical Journal*, March 1, 1873,—death from absorption by a wound four inches long; *New York Medical Gazette*, April, 1871; *British Medical Journal*, 1868, p. 220,—two fatal cases; *Med. Times and Gaz.*, 1878, ii. p. 461; *Wien. Med. Wochenschrift*, 1879, xxix. 1233.

The diagnosis of carbolic acid poisoning during life ought in most cases to be practicable; for, although the symptoms simulate some forms of apoplexy too closely for the diagnosis to be made from them, very generally the odor of the drug can be perceived about the person of the victim, and close examination of the mouth will nearly always reveal traces of the local action of the acid, in the form of *white*, *hardened*, or *corrugated* patches of mucous membrane. Either these, or a *blackish urine* in conjunction with the symptoms, are diagnostic. After death a strong odor of carbolic acid can almost always be perceived when the body is opened, and the mucous membrane of the stomach affords very reliable evidence as to the cause of death. According to Dr. A. Hiller, the urine of carbolic acid poisoning as first passed varies from a clear yellow to a golden yellow, and upon standing in the air becomes dark olive and finally often blackish green. Sometimes it is grass-green, but it may appear to be normal (case, *Schmidt's Jahrb*, Bd. ccii., p. 238). This carbolic acid urine, if treated with nitric acid and afterwards with potassa, becomes, after a certain degree of concentration, blood-red or brown-red, changing through pea-green to violet. Carbolic acid mixed with urine does not answer this test (*Schmidt's Jahrbücher*, Bd. clxiv. p. 144).* The absence of carbolic acid urine proves that the case is not one of poisoning. Baumann and Hueter declare that the earliest symptom of the poisoning is disappearance of the sulphates from the urine (*Zeitschr. f. Physiol. Chem.*, i.).†

In a case of carbolic acid poisoning emetics are generally useless, owing to the paralysis of the stomach which exists, and the stomach-pump must be employed to empty the viscus. Alkalies in excess are of some value, according to Husemann, who employs a saccharate of lime,‡ and the free ingestion of oils was formerly recommended, but to Baumann and Hueter (*Med. Times and Gaz.*, ii., 1878) belong the credit of discovering the proper antidote to carbolic acid. They found that during carbolic acid poisoning the sulphates disappear from the urine, and that if a soluble sulphate be given freely to an animal poisoned with carbolic acid, the latter was converted into a harmless sulpho-carbolic acid.* Sonnenburg found that in patients presenting the dark-colored urine and other symptoms of poisoning resulting from the too free external use of the acid all trouble disappears upon the administration of the sulphate of sodium. Dr. D. Cerna (*Philad. Med. Times*, ix. 593) has, in an elaborate series of experiments upon animals, employed the sulphate of magnesium with entire success, so that it may be considered established that a *soluble sulphate* is the proper *antidote* to carbolic acid, and that it should be employed very freely and in all stages of the toxæmia, as being capable of neutralizing the poison in the blood. The chemical history of phenol inside of the body (see p. 678) explains why the sulphates are so efficient. Dr. De La Bate (*Bull. Gén. Thérap.*, cv. 418) affirms that he obtained very happy results in one case of carbolic acid poisoning from inhalations of oxygen. Dr. Jos. Szydlowsky saved a pulseless and apparently dying child ten hours after the ingestion of the carbolic acid, by hypodermic injections of ether and the administration of dilute sulphuric acid and sulphate of sodium (*St. Petersburg Wochenschrift*, 1883, x. 87). So long, therefore, as a patient can swallow, the antidote of carbolic acid should be given.

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* For method of detecting carbolic acid in urine, see *Lond. Med. Rec.*, 1877, p. 455.

† To detect the diminution of sulphates in the urine, remove any albumen present by boiling, acidify with acetic acid, and add chloride of barium in excess. This reagent gives a milky cloud of sulphate of barium in the presence of sulphates, but a mere haze or no alteration in carbolic acid poisoning.

‡ Dissolve sixteen parts of sugar in forty parts of distilled water, and add five parts of caustic lime; digest for three days, stirring from time to time, filter, and evaporate to dryness. The product thus obtained dissolves easily in water.

Carbolic Acid as an Antiseptic and Germicide.—In 1870, Grace Calvert proved that albumen was preserved for eleven days when mixed with carbolic acid, and Dr. John Dougall that one twenty-five-hundredths part would destroy spermatozoa and the higher infusoria. Schroeter, in 1878, found that 0.0501 per cent. (one in two thousand) would keep flesh for four weeks and 0.2 per cent. permanently. It was soon found that the acid acted even more powerfully upon moulds than upon putrefactive organisms.

The first to study the action of carbolic acid upon vaccine lymph were Braidwood and Vacher, and their experiments have been repeated and extended by Dougall, by J. W. Miller, by Hoppe-Seiler, and by Baxter. Each of the last two observers found that two per cent. of the carbolic acid destroyed with certainty the infective power of vaccine, a conclusion on the whole not discordant with that of the other observers.

The germicidal power of the drug has also been studied by Hugge, Rosenbach, Baxter, Sternberg, Davaine, Koch and Blyth, Arloing, Cornevin, Thomas, and various other observers upon almost all of the known forms of infective organisms.

Their concordant testimony shows that one per cent. in an aqueous solution will destroy with certainty the virulence of ordinary septic and purulent matters, of the tubercle bacillus, and of the micrococci of fowl cholera; some of the organisms related to putrefaction have also been destroyed by solutions of this strength. But to produce these results in some instances the contact with the disinfectant had to be continued for many hours. Two per cent. of the acid in an aqueous solution was required to destroy the infection of vaccine or of glanders.

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* For a study of sulpho-carbolic acid, see *L'Tribune Méd.*, Juillet, 1884, 328. M. F. Vigier affirms that whilst not poisonous to the higher animals it is an active antiferment. M. Rabuteau (*Compt.-Rend. Soc. Biol.*, iii., 1882, 42) finds that the acid is simply a feeble purgative.

There are, it is true, some experiments which seem to be discordant with these results, especially those of Notter and of Jalan de la Croix, who found that as much as ten to thirty per cent. of the acid was necessary to prevent the movements of bacteria in putrid infusions of beef; but there was probably some error in their experimental methods.

As a vapor carbolic acid seems to act very feebly as a disinfectant or germicide, and it is very evident that the popular estimate of the value of carbolic acid is too high.

ACIDUM SALICYLICUM—SALICYLIC ACID. U.S.

Salicylic acid has long been known to chemistry, but has only very recently been rendered available by Prof. H. Kolbe, who discovered that it could be prepared by treating a solution of carbolic acid in caustic soda with carbonic acid at a moderate heat. It occurs in long acicular crystals or in the form of a white, dull powder, of a peculiar pungent odor, and a mild, peculiar taste, accompanied by a transient sense of numbness.

It is soluble in three hundred parts of water, and in four parts of alcohol. By warming, glycerine can readily be made to dissolve four grains to the drachm; no precipitation occurs on cooling.

PHYSIOLOGICAL ACTION.—When salicylic acid is given to man in doses just sufficient to manifest its presence, symptoms closely resembling cinchonism result. These are fulness of the head, with roaring and buzzing in the ears. After larger doses, to these symptoms are added distress in the head, or positive headache, disturbances of hearing and vision (deafness, amblyopia, partial blindness), with excessive sweating. According to Reiss (*Berliner Klin. Wochenschrift*, 1875, p. 674), decided fall of temperature without alteration of the pulse also occurs; but this is denied by other observers. The action upon the system of the acid and of its sodium salts (also ammonium salt, Martenson, *Petersb. Med. Zeitschrift*, 1875, p. 343) appears to be identical, and, as several cases of poisoning with one or other of these agents have occurred, we are able to trace the toxic manifestations. Along with an intensification of the symptoms already mentioned, there are ptosis, deafness, strabismus, mydriasis, disturbance of respiration, excessive restlessness passing into delirium, slow laboring pulse, olive-green urine, and involuntary evacuations. In some cases the temperature has remained about normal, but in others has approached that of collapse. The respiration appears to be almost characteristic; it is both quickened and deepened. In some cases the dyspnœa has been extreme, and given rise to the most violent respiratory efforts. The suggestion of Dr. Hastreiter (*Med.-Chir. Corresp. Blatt*, Buffalo, Mai, 1884) that this dyspnœa is due to pulmonary congestion produced by cardiac weakness is plausible. Sweating usually is very free, and the urine early becomes albuminous. Various local evidences of vaso-motor weakness may supervene, such as rapidly appearing bed-sores at points subjected to pressure, and transitory dark-colored maculæ on various parts of the body.* In several cases death was probably produced by the acid. The most conclusive case is that of H. Quincke (*Berlin. Klin. Wochenschr.*, xix. 710). The chief post-mortem change was a breaking down of the blood, congestion of most of the viscera, and ecchymoses on the serous membranes.† In certain cases the mental disturbance has been strangely prolonged, lasting for eight days. In some instances it is cheerful, in others melancholic in type. It is stated that upon drunkards the acid acts very unfavorably, violent delirium being an early symptom of its influence. When given to dogs by the mouth in large doses, salicylic acid is said to be usually vomited. According to Laborde (*Bull. de Thérap.*, xciii. 276), when from four to five grammes of the salicylate of sodium are injected into the veins of the dog, the first result is a slight acceleration of the heart's action and of breathing, some efforts at vomiting, quietude, loss of muscular strength, with a decidedly ataxic gait, hebetude, stupor, and finally sleep. When death occurs, it is preceded by dyspnœa and general convulsions. Köhler is probably correct in attributing it to asphyxia. After these general considerations, we can probably best get an idea of the physiological action of the drug by studying its influence upon the various systems in detail.

Circulation.—In regard to the action of salicylic acid upon the *arterial pressure*, observers are so much at variance as to leave the subject enveloped in mystery. Köhler (*Centralb. f. Med. Wissensch.*, 1876, pp. 163, 195) affirms that when salicylic acid or salicylate of sodium in solution is injected into the jugular vein, there is an immediate fall of blood-pressure, which after a large dose is very pronounced; in a short time the pressure rises to some extent, but not to the normal point, whilst the pulse-waves become excessively high and two or three peaked. As he found that the fall of pressure occurred after section of the depressors, vagi, and the cervical cord, he very naturally concluded that it was due to an action upon the heart itself.*

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* For cases, consult *Deutsches Archiv für Klin. Med.*, xix., p. 319; *Centralblatt für Chirurgie*, 1877, p. 278,—401 grains salicylate of sodium taken in twelve hours; *London Lancet*, 1876, 2, 681; *Berlin. Klin. Wochenschrift*, No. 4, 8, 1876; and *Bull. Thérap.*, 1877, xciii., p. 25.

† In the case recorded in the *Virginia Medical Monthly*, June, 1877, forty-eight grains of the acid were taken in four hours. The symptoms were violent vomiting, headache, total unconsciousness, with stertorous breathing. Death occurred forty hours after the first dose. See also *Medical and Surgical Reporter*, 1878. There is no probability that in the alleged case of poisoning reported by Dr. Frank Ogston (*Brit. Med.*, 1883, i. 869) the salicylate had anything to do with the untoward symptoms or result. The case reported by Dixneuf (*Thèse*, Paris, 1878) I have not had opportunity of examining; also that of Empis and Gubler (*Bull. de l'Acad. Méd.*, 1877).

In 1879 (*Thèse de Paris*), Hugues Oltremare found that moderate doses of the salicylate of sodium increase the arterial pressure and the frequency of the pulse, whilst poisonous doses strongly depress the heart-force and the blood-pressure. In accord with this are the elaborate experiments of Danewsky (*Arbeiten Pharm. Laborat.*, *Moskau*, i. p. 190). He found that at first the arterial pressure was increased, partly on account of an increase in the force and energy of the cardiac beat, but chiefly as the result of excitation of the vaso-motor centre. Vaso-motor spasm was shown to be the main factor in the rise of the blood-pressure, by the inability of the drug to increase the arterial pressure after section of the spinal cord. The action on the heart was seemingly direct. The arterial pressure slowly fell during the later stages of poisoning, the heart-stroke becoming weaker and weaker, and finally being extinguished.

With our present evidence it appears probable that the fall of arterial pressure observed by Köhler was due to the use of very large doses, and that moderate doses have no depressing effect upon the circulation. Clinicians have, I think, generally come to the conclusion that the drug is depressant to the heart in man, and not to be used when cardiac weakness exists. This is, however, earnestly combated by E. Maragliano (*Zeitschrift f. Klin. Med.*, 1884, viii. 248), who has made a very large number of sphygmographic studies, and also a series of experiments with the sphygmomanometer of Basch, and finds the arterial pressure usually elevated, and never depressed, by therapeutic doses of the drug. It is possible that the general nervous depression which the drug—given very largely—produces has been mistaken by clinicians for a cardiac depression, but it must be remembered that when given continuously the salicylates probably accumulate in the system, and may reach the amount necessary to depress the heart.

Nervous System.—Our knowledge of the action of the drug upon the nervous system is very imperfect. According to Sée, the violent convulsions that precede death are in the lower animals almost the sole evidences of disturbance of the nervous system, neither the reflex power of the spinal cord, the general sensibility, nor the conducting power of the nerve-trunks being affected. M. Bochefontaine affirms, however (*Le Progrès Méd.*, 1877, p. 630), that in the frog the drug acts as a paralyzant, destroying the functional power of the spinal centres, whilst according to M. Laborde four grammes of a salicylate will produce in the dog profound cutaneous anæsthesia (*Ibid.*, 609).

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* Prof. Sée (*Bulletin de l'Académie de Médecine*, 1877, p. 697) states that in his experiments there has been no action whatever upon the arterial pressure or on the pulse-rate; but there is reason for believing that these negative results were reached, because Prof. Sée gave the acid by the mouth and cited the blood-pressure before the drug was absorbed, since Köhler found (*loc. cit.*) that injections of solutions of the acid into the stomach of dogs and rabbits failed to affect the blood-pressure, although the sodium salt administered in a similar manner did depress the force of the circulation.

Respiration.—In Köhler's experiments upon rabbits and Danewsky's experiments upon dogs, the *respiration* during the injection of the acid or its sodium salt into a jugular vein was decidedly quickened, but after a time the rate fell to much below the normal. When, in Köhler's experiments, the pneumogastrics were divided during the period of retardation, the frequency of the respiration was still further lessened. Danewsky practised section of the vagi before exhibiting the drug and during the first stage of accelerated breathing. In the first instance he found that the breathing was only slightly accelerated by the drug; in the second that the quickened respiration fell to the same slowness that is seen in the unpoisoned animal with cut pneumogastrics. His experiments were too few to be conclusive, but indicate the correctness of his deduction, that the quickening of respiration is largely due to an irritation of the pulmonary vagi, and not solely to an influence upon the respiratory centres. There is, however, probably some stimulation of the respiratory centres after small doses, but after very large doses fatal failure of respiration occurs through a gradual or sometimes sudden depression of the centres.

Temperature.—Especial interest attaches to the action of salicylic acid upon the temperature. In Prof. Sée's experiments upon normal men and upon animals, very large doses (ten grammes for men) had no effect upon the temperature (*loc. cit.*, p. 697). The experiments of Dr. Paul Fürbringer upon rabbits, dogs, and men are in accord with this (*Zur Wirkung des Salicylsaüre*, Jena, 1875). M. Gedl, in twelve seemingly very carefully conducted experiments upon man, in which the doses varied from forty-six to seventy-eight grains, found that the effect in three cases was various, in two cases negative, in three a lessening of the daily alterations of temperature, in three a slight lowering of temperature, and in one a fall of 0.8° C. (*Centralblatt f. Med. Wissensch.*, 1876, p. 403). Danewsky states that in normal animals and man the influence of the acid upon temperature is slight and inconstant. The evidence seems to show that salicylic acid, like quinine, has, in non-toxic doses, little or no decided action upon the temperature in health. In one or two experiments upon himself, Mr. North (*Practitioner*, xxiii. 184) found that the acid exerted a decided influence in preventing the rise of bodily temperature normally caused by exercise.

The original article of Dr. E. Butt upon the action of salicylic acid upon temperature in fever has been followed by a number of papers (see *London Med. Record*, 1876, p. 193*), which show that the drug fails in some cases, and should never be used to the exclusion of the cold bath and other similar remedies, but seems to be more certain and decided in its effects than is quinine; although the latter is denied by some practitioners who have used both drugs.

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* Consult also *Deutsches Archiv für Klin. Med.*, 1876, xv. 457, 518, 612, xvi. 162, xvii. 294, 314, 607, 692, xviii. 401, 452, 504; *Centralblatt für Med. Wissensch.*, 1876, xci. 198; *London Lancet*, 1877, ii. 812; *London Practitioner*, xvi. 200; *Lond. Medical Record*, 1877; *Berlin. Klinische Wochenschrift*, 1875, 693; *Le Progrès Méd.*, 1877; *Bulletin de l'Académie de Médecine*, 1877. For information in regard to its action on pyæmic rabbits, see Fürbringer, *loc. cit.*

The first effect of a single antipyretic dose in fever is usually a profuse sweat, which may appear fifteen minutes after the ingestion of the remedy (Ewald, *London Practitioner*, vol. xvi. p. 200). Very shortly after this the temperature begins to fall, and, according to Justi (*Centralblatt für Chirurgie*, 1876, p. 629), the depression reaches its maximum in about six hours. The sweating is profuse and exhausting, amounting, according to Ewald, not rarely to seven hundred and fifty grammes. The perspiration can scarcely be the only factor in the reduction of temperature, as there appears to be no relation between its amount and the degree of the fall, and it usually ceases before the latter reaches its maximum.

The statements in regard to the action on the pulse in fever vary so much as to suggest that when any decided lessening of the cardiac beat does occur, it is dependent upon the fall of temperature. Thus, Garcin (*Journ. de Thérap.*, 1876, p. 25), Oulmont (*Le Progrès Méd.*, 1877, p. 587), Moeli (*Deutsches Archiv.*, xvii. p. 592), have all observed the pulse-rate to fall with the fever-heat, whilst L. Schroeder affirms that after moderate doses the pulse is slackened, after large ones quickened, and Ewald and other observers state that it is usually not affected. The antipyretic dose employed varies somewhat. Ewald gives as a minimum to the adult seventy-five grains, repeated in five hours if necessary; Justi, from ninety to one hundred and twenty-five grains.

Absorption and Elimination.—Salicylic acid appears to be absorbed very rapidly. Drasche (*Centralbl. Chir.*, 1876, p. 777) affirms that it is only necessary to apply its alcoholic solution to the sound skin for a short period, in order to find the drug in the urine. Owing to the insolubility of salicylic acid, the problem of the method of its absorption and of the state in which it circulates in the blood early attracted attention. Salkowski (*Berlin. Klin. Wochens.*, 1875, p. 297) pointed out that the acid in the blood probably exists in the form of a salicylate of sodium. Prof. Binz supposes (*Lond. Prac.*, xxvi. p. 443) that the acid is liberated in the blood by the carbonic acid formed in the tissues. The only basis for this theory consists in the fact that, by passing carbonic acid gas through a solution of phosphate, carbonate, and salicylate of sodium, agitating with ether, and separating and evaporating the latter, crystals of salicylic acid are obtained. It is evident that if in the blood changes take place similar to those which occur in this solution, salicylic acid should be yielded to ether shaken with the blood of an animal poisoned with the drug. Feser and Friedeberger found that unless enormous doses of the drug were injected into the blood so as to produce immediate violent convulsions and death, the vital fluid of the poisoned animal yielded nothing to ether. In Köhler's experiment (*Centralbl. für Med. Wissens.*, 1876, p. 553), when salicylic acid was dissolved in normal blood no acid was yielded to ether, but when the blood of asphyxia, *i.e.*, blood supersaturated with CO_2, was employed, a very notable amount of the acid was extracted by the ether. The theory of Prof. Binz is certainly not proven, and is probably incorrect.

Feser and Friedeberger (*loc. cit.*) have advanced the theory that the salicylic acid circulates in the form of an albuminate. This has received some support from the experiments of Farsky (*Sitzb. d. k. Akad. d. Wissens.*, lxxiv., Bd. ii.), which seem to show that the acid is capable of forming such a compound.* On the other hand, the theory is contradicted by the results of Fleischer (*Med. Centralbl.*, 1876, p. 628), who digested albuminous solutions with the acid, and after coagulation by heat found all the acid in the filtrate; and who also treated the blood of poisoned animals in a similar way, and found the salicylic acid only in the serum, the coagulum being free.

Viewing all this evidence together, it seems a probable conclusion that salicylates, when administered internally, enter the vital fluid and circulate there as salicylates, and that salicylic acid itself is probably converted by the alkaline juices of the alimentary canal into a salt, and as such enters the system and exerts its influence on the organism.

Salicylic acid escapes from the body chiefly through the kidneys.† Fürbringer and Drasche (*Centralbl. Chir.*, 1876, 777) failed to detect it in the fæces, the saliva, bronchial secretion, or the sweat, but M. Mussy found it in the saliva (*Bull. Thérap.*, xiii., p. 318), as did also M. Balz; and M. Oulmont detected it in the serosity of a blister. It appears in the urine very soon after its ingestion, but its elimination proceeds slowly. Thus, in a case of exstrophy of the bladder it was detected in the urine dripping from the ureters eight and a half minutes after its ingestion (Balz, *Arch. d. Heilk.*, xviii., S. 60), and it has been found in the urine eight days after the exhibition of the last dose (Byanow, *Centralbl. für Chir.*, 1877, p. 809). The latter observer also found it in the urine of a normal man as a salicylate twenty-five minutes after its swallowing. The same authority states that it is excreted partly as salicyluric acid,‡ partly as a form of salicin, and he believes to some extent as oxalic acid. Urine which had been passed some hours after the ingestion of a dose polarized to the left. Dr. A. E. Stuart (*Lond. Practitioner*, xviii., p.

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* He digested various albuminous substances with salicylic acid, washed them with ether until it would take no more acid, dried, washed with water, and found on analysis salicylic acid largely present in the residue.

† To detect salicylic acid in the urine add the solution of chloride of iron carefully. At first white phosphate of iron precipitates, then, if the acid be present, a violet color is produced (Kolbe).

‡ Salicyluric acid is a parallel compound to hippuric acid, made by the union of the elements of a glycocol with salicylic acid.

425), after so small a dose as nine grains of the acid, saw free, distinct crystals of salicyluric acid in the urine. It is possible that such of the salicylic acid as escapes unchanged from the kidney may, as first excreted, be in the form of a salicylate, but be set free by the phosphoric acid of the urine; at least such would be indicated by the fact that in Balz's case of exstrophy salicylate of sodium appeared in the urine twelve minutes before the free acid. The green color of the urine characteristic of the free use of salicylic acid appears to be due to an increase in the formation of indican (S. Wolfberg, *Deutsch. Archiv f. Klin. Med.*, xv., p. 403; M. Robin, *Lond. Med. Record*, 1877, p. 151), or else to pyrocatechine (see *Bull. Acad. Méd.*, 1877, p. 705), and it is not improbable that the pyrocatechin is formed out of the salicylic acid. The urine itself is often augmented in quantity, but sometimes it is diminished. It not rarely contains albumen, evidently the product of a local irritation of the kidneys. Sée reports (*loc. cit.*, p. 705) a case in which the renal irritation was so severe as to give rise to hæmaturia. In regard to the solids of the urine, the testimony varies somewhat. Sée (*loc. cit.*) affirms that in gout the uric acid is greatly increased, and that both in health and disease the urea is unaffected. S. Wolfsohn (Inaug. Diss., quoted in *Centralbl. f. Med. Wissens.*, 1877, p. 30), on the other hand, determined an increase in the nitrogenous renal elimination, whilst Lecorché and Salamon have found that when the acid is exhibited in rheumatism there is at first an enormous increase in the excretion of both urea and uric acid, followed by diminution, which may carry the elimination below the normal. In acute rheumatism the first increase lasts three or four days, in subacute rheumatism one or two days; excretion of phosphoric acid is also at first increased and subsequently lessened. In experiments upon dogs Carl Virchow found that the nitrogenous elimination was increased by the salicylate of sodium (*Zeitschr. f. Physiol. Chem.*, vi. 78).

THERAPEUTICS.—The known physiological action of salicylic acid would only lead to one use of it in internal medicine, namely, as an antipyretic. The question as to whether good is achieved in fevers by its administration is, of course, entirely separate from that as to its power of reducing temperature. It is certainly possible for a drug to lower the fever-heat, and yet to do far more harm than good, and the evidence at hand does not yet seem sufficient to answer the present inquiry. In the Semenoffschen Military Hospital, from January, 1875, to the middle of September, 1875, two hundred and eleven cases of typhoid (?) fever were treated without salicylic acid, and from the last date to March, 1876, one hundred and sixty cases with the acid. The mortality in the first period was 14.7 per cent., in the last 19.4 per cent. (Schroeder, *Deutsches Archiv für Klin. Med.*, xviii., p. 516). In the garrison of Stargard, in 1872, thirty-nine cases received mild cold-water treatment; in 1874, sixty-three cases, cold-water treatment energetically; in 1875, thirty-five cases, the salicylic acid treatment; the mortality being, respectively, 30.7, 9.5, 8.5 per cent., and the average length of treatment

66.6, 53.3, and 37 days (Jahn, *Ibid.*, p. 451). Riess treated 260 cases of typhoid fever, and lost 24.2 per cent. (*Berlin. Klin. Wochens.*, xii., p. 675). He asserts that the duration of the disease was very much shortened. These statistics are all that are at command, and certainly leave the question at issue *sub judice*. My own feeling is that salicylic acid will be found to do more harm than good in such diseases as typhoid fever.

The *antiperiodic* action of the drug does not appear to be such as to entitle it to confidence. It is true that Senator in nine cases of *intermittent fever* had but one failure (*Berlin. Klin. Wochens.*, 1875); but the general drift of experience coincides, we think, with that of Helley, who found salicylic acid to fail in obstinate malarial cases, and in mild cases to require longer time to cure than does quinine.

The antipyretic properties of salicylic acid early led to its being* used in *rheumatism*, and in 1876 (*Berlin. Klin. Wochens.*, xiii.) Stricker first announced that it was an exceedingly valuable remedy in this disease, usually, when given in hourly doses of from seven to fifteen grains, causing a disappearance of the symptoms in a period not exceeding forty-eight hours. The conclusions of Stricker have been substantially confirmed by numerous observers in Germany, France, England, and this country. Although some cases of rheumatism do not seem to yield to the drug, in the great majority of instances improvement sets in within twenty-four hours, and is rapidly followed by disappearance of the pain and fever. The dangers of cardiac and cerebral complications are certainly lessened, but not altogether done away with.† In excessive *rheumatic hyperpyrexia* it cannot be depended upon to the exclusion of the cold bath. Jaccoud states (*Progrès Méd.*, 1877, pp. 528, 745) that he has found it of great service in *chronic rheumatism;* but the general testimony appears to show that it is much less certain in the chronic than in the acute disorder. Jaccoud also states that in acute *gout* it acts with extraordinary effect. As in cases of habitual gout the kidneys are often seriously affected, the urine should always be examined, and if it be found albuminous the remedy be withheld. Various mishaps (gangrene, *Bull. de Thérap.*, xciii., p. 324; necrosis, *British Medical Journal*, 1876, pp. 2, 776, 820, 843) have been ascribed to the use of the acid in rheumatism, but these were in all probability accidental complications of the disorder. Delirium and temporary insanity, sometimes erotic, have been in various cases, perhaps correctly, attributed to the acid (*New York Med. Record*, xxi. 456; *London Med. Record*, 1882, 452). Dr. H. Weber has seen the salicylates act most happily in *gonorrhœal rheumatism* (*Bull. de Thérap.*, xciii. p. 328).

In *diphtheria* locally applied and exhibited internally the remedy has been highly commended. In chronic *cystitis* with ammoniacal urine, and in chronic *pyelitis*, it is often of service.

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* E. Buss was probably the first one to make trial of this remedy.

† Consult for this point Jaccoud (*Le Progrès Méd.*, 1877, p. 588), Green (*London Lancet*, Nov. 11, 1877), Roe (*London Lancet*, 1877, 2, p. 905), Jacobs (*Ibid.*, 655), Brown (*Boston Med. and Surg. Journ.*, Feb. 8, 1877).

ADMINISTRATION.—The maximum dose of salicylic acid in acute rheumatism may be set down as a drachm in the twenty-four hours, although it is employed by some practitioners in much larger doses. The *salicylate of sodium* (*Sodii Salicylas*, U. S.) contains forty-eight grains of the acid to the drachm: since it is freely soluble in water, and is less unpleasant to the taste and less irritant to the stomach, it is much preferable to the uncombined acid. From sixty to eighty grains of it may be administered in the course of the day in a strongly aromatized syrup. If ringing of the ears or other evidences of intoxication appear, the remedy should at once be partly or entirely withdrawn.

Use as an Antiseptic.—Salicylic acid was originally brought to the notice of the profession on account of its inhibitory influence on putrefaction. Kolbe found that .04 per cent. had great influence in preventing souring of milk.

Bucholz found that 0.15 per cent. of the acid is sufficient to prevent the development of bacteria in ordinary organic mixtures, and that the influence of 0.005 per cent. is plainly visible; 0.3 to 0.4 per cent. of the acid killed bacteria in vigorous growth (*Arch. Exper. Path. u. Pharm.*, Bd. iv.). The salicylate of sodium was about equal to the pure acid, 0.4 per cent. destroying the bacteria.* In the preservation of urine, Meyer and Kolbe found that one part of salicylic acid to two thousand of urine was sufficient to prevent putrefaction (*Journ. für Prakt. Chem.*, Bd. xii.). According to Prof. Kolbe and others, salicylic acid arrests or prevents the action of the non-organized organic ferments. Thus, it will forbid the action of emulsin upon amygdalin or upon myronic acid, and prevent the development of hydrocyanic acid or of the volatile oil of mustard. Dr. Miller found that one per cent. of salicylic acid was sufficient to check the action of ptyaline upon starch; for the same effect ten per cent. of carbolic acid was required. The digestive action of pepsin, outside of the body, was very seriously affected by 0.2 per cent. of salicylic acid in Dr. Miller's experiments, but in Kolbe's experiments the ingestion of twenty grains a day of the drug had no effect.

There can be no doubt that salicylic acid is capable of accomplishing much in antiseptic surgery, but it does not seem to be replacing carbolic acid, as it at one time bid fair to do. Its freedom from odor and comparative freedom from poisonous and irritant properties are certainly strong recommendations in its favor; nevertheless, carbolic acid is more generally employed, and Mr. Callender, after twelve months' trial in the wards of St. Bartholomew's Hospital, has formally condemned salicylic acid as much inferior to carbolic acid (*Trans. London Clin. Soc.*, ix.). Thiersch's *salicylic acid wadding* for hermetically sealing wounds is made by dissolving two ounces of the acid in two pints of alcohol (sp. gr. 0.83), diluting with twenty pints of water at 158° to 178° F., saturating with this six pounds and eight ounces of cotton batting deprived of oily matter, and afterwards drying. This wadding contains three per cent. of the acid; for some purposes a stronger batting, containing ten per cent., is prepared. When the wound or abscess is discharging profusely, jute is substituted for the cotton batting, because it is much more permeable to pus. An efficient ointment may be prepared by dissolving one and a half parts of the acid in two parts of alcohol and adding lard, or the solubility of the drug in glycerine may be taken advantage of.

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* The power of the acid has been denied by Fleck (*Benzoesäure & C., Munich*, 1875), who has been abundantly answered by Prof. Kolbe (*Journ. für Prakt. Chem.*, Bd. xii.).

The following solutions are used in St. Bartholomew's Hospital: Phosphate of sodium, three parts; salicylic acid, one part; water, fifty parts.—Salicylic acid, one part; olive oil forty-nine parts.—Salicylic acid, one part; bicarbonate of sodium, half part; water, one hundred parts.—Salicylic acid, ten parts; borax, eighteen parts; water, one hundred parts. A twenty-five per cent. solution, which will bear dilution with water or alcohol, may be prepared according to the following formula: ℞. Acid. salicyl., ʒii; Sodii biborat., ʒi; Glycerinæ, q. s.

Mix the acid and borax with four fluidounces of glycerine; heat gently until dissolved; then add enough glycerine to make one fluidounce. Prof. Thiersch has found that the drug cannot be employed for cleaning surgical instruments, because it corrodes the steel.

SALICINUM—SALICIN. U.S.

Salicin is obtained from the bark of the willow and other trees. It occurs sometimes in tabular crystals, more frequently in white, shining needles of neutral reaction, soluble in about thirty parts of cold water, very soluble in hot water and in alkaline solutions. Concentrated sulphuric acid dissolves it, with the production of a beautiful red color. By carefully warming it with dilute sulphuric acid it is converted into glucose and *saligenin*, and it is therefore a glucoside.

The action of salicin upon the animal organism is not known, but would seem to be very feeble, as Ranke (*Pflanzenstoffe*, p. 903) is said to have taken nearly three ounces of it without any notable effect. It is certainly rapidly absorbed, probably as salicin; but once in the blood it seems to be quickly decomposed, the products of its change appearing in the urine fifteen to thirty minutes after the ingestion of a single dose. This change does not appear to be complete, as, according to Husemann (*Pflanzenstoffe*, 963), in the urine of man and rabbits after the ingestion of salicin not only saligenin and salicylic acid but also unchanged salicin occur. Further, Falck, injecting salicin into the blood of the dog, found that it chiefly escaped from the kidneys unaltered. The elimination seems to go on slowly, as Senator has detected salicylic acid in the urine sixty hours after the ingestion of a single dose of salicin (*Berlin. Klin. Wochens.*, 1877, 181).

In 1874, Dr. Maclagan, led by some fancied dependence of rheumatism upon malaria, began the use of salicin in acute rheumatism, and in 1876 (*Lancet*, 1876, i. 342) announced that it was a specific remedy, rapidly abating both the fever and the local symptoms. In the same year (*Centralb. Med. Wissens.*, 1876, 241; also *Berlin. Klin. Wochens.*, 1877, 181) H. Senator confirmed these statements, and further affirmed that in various affections he had found salicin to have an antipyretic power entirely comparable to that of salicylic acid. If these views are correct, the freedom from irritant properties and disagreeable taste made salicin superior to the acid. The only person, other than those mentioned, who has tested the matter on a considerable scale, is Dr. Buss, who does not find that the drug is nearly so powerful as salicylic acid (*Berlin. Klin. Wochens.*, xiii. 504). If, as is believed by Senator, the activity of salicin depends upon its conversion in the blood into salicylic acid, it is plain that its action should be slower and more uncertain than that of the acid.* Further investigations are necessary before any conclusion can be reached; but the later evidence does not seem to be so favorable to salicin as do the reports of Maclagan and Senator. In regard to the dose employed, it is worthy of remark that no serious symptoms have been reported as produced by salicin. Senator recommends two to two and a half drachms as a moderate dose for the adult. Maclagan used much smaller doses,—twenty grains every three hours.†

THYMOL. U.S.

Thymol is found in the oil of thyme and of some other plants. It occurs either as an uncrystallizable liquid or in white rhombic or acicular crystals. It has been used with satisfaction as a substitute for carbolic acid by Volkmann and Ranke, of Halle, and other practitioners, but, although it is undoubtedly powerfully antiseptic, does not seem to have rapidly gained favor. Its fragrant odor has proved a decided disadvantage, in summer at least, by attracting swarms of flies. It is not free from poisonous properties. On the other hand, it is claimed that it does not irritate the skin, and has a decided influence in preventing discharges. Spencer Wells employs its watery solution (1 to 1000 of warm water); Volkmann, thymol 1 part, glycerine 20 parts, alcohol 10 parts, water 1000 parts. It has been used internally by Bälz (*London Med. Record*, 1878) in doses of thirty grains a day, or less. In a few instances nausea and vomiting were caused. There was abundant sweating, singing in the ears, deafness, constriction in the forehead, reduction of temperature, and frequently diarrhœa. The urine was dark greenish, yellowish brown by transmitted light, free from albumen, becoming cloudy and grayish white on the addition of the tincture of the chloride of iron. Violent delirium occurred several times, also marked collapse, and, in one case of typhoid fever, unconsciousness, with most alarming collapse. Dr. Bälz concludes that the remedy is much less certain and more dangerous as an antipyretic than is salicylic acid. The possession of poisonous properties by thymol has been confirmed by the recent experiments of Dr. B. Kuessner (*Med. Times and Gaz.*, Dec. 1878, p. 716). This observer found that when given to dogs and rabbits by the stomach the poison acts very slowly and feebly, on account of its slow absorption, but that when injected into the circulation it produces death by failure of respiration. Coma is developed some time before death, and the blood-pressure, which at first maintains itself, now falls steadily. Post-mortem examination failed to detect fatty degeneration or other lesion in either the solid tissues or the blood. The continuous repeated exhibition of small doses of thymol had no perceptible effect, except to in some way interfere with nutrition, so that the animals lost flesh.

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* Dr. Maclagan asserts (*London Lancet*, 1872, ii. 179) as proof that salicin does not act as salicylic acid, but as salicin, that he has given salicin to rheumatic patients suffering from cerebral symptoms due to large doses of salicylic acid, and seen both the rheumatism and cerebral disturbance abated; is it possible the delirium in these cases was due to rheumatic irritation and not to the salicylates?

† Consult also *Brit. Med. Journ.*, ii. 1876, and *Boston Med. Surg. Journ.*, Feb. 1877.

The evidence already forthcoming indicates that the therapeutic use of thymol will be very limited. Its costliness and the absence of marked advantages in its favor militate against its being largely used externally. There is, however, one local employment of it which is important,—namely, as a detergent antiseptic in various ulcerated and diseased conditions of the mouth. For such use its agreeable taste and odor pre-eminently fit it. That anything whatever is to be gained by its internal administration is not at all certain. Enough has been said to condemn it as antipyretic. Kuessner found the sugar in the urine of a patient with *diabetes* reduced by from one to two grammes thymol per diem; but Fürbringer (*Deutsches Archiv fur Klin. Med.*, xxi.) reports a case in which one gramme daily increased the sugar. Kuessner thinks thymol (three to five minims of a 1 per cent. solution three times a day) of value in *vesical catarrh* and in *infantile diarrhœa*, and found that inhalations (one part to 1000) diminish the fever and expectoration of *phthisical* patients.

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[*] According to a statement in *Hoffmann und Schwalbe's Jahresb.*, 1879, 208, Küssner has found that thymol has the power of dissolving the red blood-corpuscles.

ANTIPYRIN.

This is a substance discovered by Dr. Ludwig Knorr, of Munich, and first experimented with by Professor Filehne, of Erlangen (*Zeitschrift. f. Klin. Med.*, 1884, Bd. vii., 641). It is a grayish or reddish-white crystalline powder of a slightly bitter taste, soluble in fifty parts of ether, much more so in water, ten parts of it being dissolved in six parts of cold water, and also very soluble in alcohol and chloroform. Its solution strikes with a solution of perchloride of iron a reddish-brown color, with nitric acid a beautiful greenish color. Chemically, it is dimethyloxyquinizine. It is prepared by a very complicated (patented) process.

Physiological Action.—Our knowledge of the physiological action of antipyrin is very incomplete. According to the observations of Dr. Leon Arduin (Paris *Thesis*, 132, 1885), of Prof. Demme (*Fortschritte der Medicin*, Bd. ii., 1884, p. 657), and Dr. Coppola (*Kobert's Jahresbericht*, 1885, p. 314), it produces in frogs, when given in very large doses, complete relaxation, with loss of reflex action and death. In moderate toxic doses (half to one centigramme) it causes opisthotonos with very marked increase of the reflexes. In the earlier stages of this condition the animal is cataleptic. According to Coppola, the convulsions are, at least in part, due to the action upon the brain, and are arrested by section of the spinal cord. Both Arduin and Demme state that death is produced by arrest of the heart in diastole; but Coppola affirms that the antipyrin has no influence upon the circulation in the frog, and that in many cases after the largest dose the heart is arrested in systole, and that in the Williams apparatus no influence was exerted by antipyrin upon the isolated heart except after the most enormous doses.

There have been but few experiments made upon the higher animals with this drug. Demme asserts that the symptoms which it produces in rabbits are similar to those that occur in frogs. One gramme in his experiments produced in a rabbit very marked elevation of the blood-pressure, followed by violent tetanic cramps, progressive falling of the blood-pressure, and lessening of reflex excitability. In his experiments the heart continued to beat vigorously after the blood-pressure was reduced almost to zero, and death appears to have been produced by failure of the respiration. In the experiments reported by Arduin, three grammes of antipyrin produced in a rabbit cataleptic stiffness, diminished reflexes, complete paraplegia, followed by violent convulsions, epileptiform in type and occurring at a time when the reflexes were completely destroyed in the hind legs. There was also very marked fall of the bodily temperature. M. Bouchard (quoted by Arduin) has found that the stiffness of the muscles is prevented entirely by section of the sciatic nerve, and is therefore of nerve origin. In Demme's experiments upon the isolated frog's heart, antipyrin rapidly slowed and enfeebled the systole. Coppola affirms that antipyrin has a very slight and temporary influence upon the sensitive nerves, and at the place of injection sensibility is lessened for some minutes. The pupils are also constantly dilated by it.

Antipyrin is freely eliminated by the kidneys. Marigliano (*Kobert's Jahresbericht*, 1885, p. 313) states that it appears in the urine three hours after its ingestion, and that the elimination is at its height in four hours, and continues for a day to a day and a half. He states that it can readily be recognized by rendering the urine acid and adding an iodized solution of iodide of potassium, when a reddish-brown color develops. The urine itself is normal in appearance, and never contains albumen. I. I. Hage (*Ibid.*, p. 316) failed to detect antipyrin in the sweat or saliva.

M. Arduin has called attention to the hæmostatic action of antipyrin, and affirms as the result of experiments that given internally its effect is similar to but more powerful than that of ergotine. The same observer has found that it has very great preservative powers, and indeed is superior in preventing putrefaction to salicylic acid. It is asserted that given in cases of phthisis it will diminish remarkably the fetidness of the expectorations.

THERAPEUTIC ACTION.—When antipyrin is given to a healthy man in a dose of half a drachm, it usually produces no marked symptoms except some singing in the ears, slight nausea, and an uncertain fall of bodily temperature, which very rarely, if ever, amounts to more than one-tenth of a degree. After doses of a drachm or upwards vomiting is very apt to occur, accompanied or preceded by giddiness and distress in the head. In fever cases, about half an hour to an hour after a dose, profuse sweat occurs, and it is at this time that the fall of temperature occurs. It does not appear, however, that the fall of temperature is produced by the diaphoresis. At least, according to Carl von Noorden (*Berlin. Klin. Wochen.*, 1884, p. 523), the sweating can be arrested by the use of hypodermic injections of atropia or agaricin without affecting the fall of temperature. According to most authorities the depression of temperature lasts longer than that caused by other antipyretics, continuing from two to twenty hours. It is accompanied by a reduction of the rate but not of the force of the pulse. In some cases the sweating is not profuse, and it is probably under such circumstances that observers have noticed a markedly increased diuresis. Most observers affirm that the patient is usually more comfortable under the action of the drug than at other times; sometimes, however, the vomiting is distressing, and the occurrence of a peculiar eruption upon the surface of the body is frequent, and is often accompanied by considerable distress. This eruption is of the character of roseola, or sometimes resembles very closely measles. In the severest cases its coming on is marked by a chill followed by fever, and it may last for four or five days.

Antipyrin has been employed as an antipyretic, with asserted very good results, in almost all of the diseases accompanied by high temperature, such as *pneumonia*, *erysipelas*, and *typhus*, *scarlet*, *yellow*, and *typhoid fevers*, *rheumatism*, etc.: it has also been freely given in the hectic fever of phthisis, but various observers state that in such cases it produces so much feebleness and general depression as to forbid its use. In *typhus fever* it reduces the temperature, but in a number of recorded cases has caused very serious collapse. Whether it has any specific action in rheumatism is at present uncertain; the testimony which we have indicates, however, that it does not in this respect at all equal salicylic acid. According to A. Pribram (*Prager Med. Wochen.*, 1884), in *pneumonia* the frequency of the respiration is distinctly lessened by it. In children it has been used with asserted good results by a number of clinicians. M. Hucard found it especially useful in the pneumonia and bronchitis of children.

Antipyrin may be administered hypodermically by the mouth or the rectum. The hypodermic injections at times produce local irritation, but are usually well borne. The dose for a child of one or two years of age may be set down as three grains; for a child five years old seven grains; for the adult the dose should not exceed thirty grains, repeated every one or two hours until from sixty to eighty grains are given, or sweating comes on. In children it would not be safe to repeat the dose more than once Some authorities prefer a single large dose of from sixty to seventy-five grains in the adult.

HYDROCHLORATE OF KAIRIN, occurring in white crystals freely soluble in water, and of a bitter, saline, and somewhat aromatic taste, has been used to a considerable extent abroad as an antipyretic. It produces, when given to a fever patient, distinct fall of temperature with excessive sweating, and greenish-colored urine. Its influence upon the temperature is rapidly produced, but rarely lasts more than three hours. In a number of cases, especially of *typhus fever*, its use has been followed by cyanosis and collapse, and it is also very apt to produce vomiting: the general testimony is that it is less powerful in its antipyretic action, and more dangerous and disagreeable in its secondary effects than is antipyrin. The dose is from five to ten grains every hour until the fall of temperature sets in. It is stated that after the fall the effect may be maintained by giving smaller doses every hour.

THALLIN, or *parachinanisols*, appears to be an exceedingly powerful antipyretic, producing a rapid fall of temperature, but also very disagreeable symptoms with a decided tendency to collapse.

PART II.

FORCES.

CALORIC.

THERE are two conditions of the force caloric, spoken of as distinct entities, but which are merely relative terms, expressive of the presence of an excess or of the absence of the normal amount, or, more strictly speaking, normal intensity, of the force. Cold and heat, in connection with the human body, mean simply an intensity of caloric below or above 98½° F.

USE OF HEAT.

The phenomena of death from cold show that a lack of caloric in the body is no less paralyzant of animal functions than is an excess of the same force. Evidently the organism was constructed to run upon a certain plane of heat, and cannot vary from this without serious results. By numerous experiments upon animals I have proven that in a cool apartment death rapidly results after section of the spinal cord, from falling of the bodily temperature, the animal which, in a warm room, will live indefinitely, dying very shortly in a temperature of forty degrees. The cause of the inability of the animal to resist external cold after section of the cord is undoubtedly vaso-motor paralysis. Normally, the temperature of the interior of the body is maintained by keeping an outer layer of partially-cooled tissue between the internal organs and tissues and the outer air. When the power of contracting the superficial vessels has been lost, the organism can no longer maintain this protecting layer, the surface temperature rises to that of the interior, heat is rapidly lost, and the whole body uniformly cooled.

Vaso-motor paralysis is produced by toxic doses of various remedies, and under these circumstances artificial maintenance of the bodily temperature is imperative, forming a most important portion of the treatment of all such *poisoning*. *Collapse* from any cause is largely dependent upon, or, more correctly speaking, largely is, vaso-motor palsy; hence, in almost all forms of collapse, the use of external heat is of great importance.

Dr. Chas. Hunter, of this city, has very successfully applied this treatment to that form of collapse which follows injuries and surgical operations, and is known by surgeons as *shock*. The lack of power of alcoholic and other ordinary stimulants in this condition is proverbial. The pathological state is undoubtedly vaso-motor palsy, the bodily temperature is much below normal, and the rational treatment consists in the hypodermic use of atropia and digitalis, and the external employment of the hot bath. I believe that this plan of treatment will be found to be a most important addition to surgical therapeutics. In the first days of post-fœtal life the power of resisting external cold is very slight, and in many cases of still-born children, or of children whose vital powers are almost extinguished at birth, life may be saved by a high external temperature, the little waif being kept in an air of 98° F., and from the influence of cold walls and articles which shall draw off, as it were, the little store of heat provided by nature, radiation being greatly affected by the temperature of surrounding objects.

It is hardly necessary to dwell in more detail upon the various forms of collapse. Enough has been said to illustrate the principle that *whenever the bodily temperature falls below normal pyretic treatment is demanded.* The vigor of the treatment should always be in direct proportion to the suddenness and extent of the fall of temperature.

In regard to the methods of applying heat, it must, in the first place, be understood that wrapping in blankets, etc., is only able to prevent cooling of the body; that when the animal temperature has already fallen it will not suffice at all. The same may be said of air heated to temperatures which can be readily obtained or can be continuously borne by the attendants. Radiated heat is somewhat better, and often the use of a brisk open fire is of service. The *hot bath* is, however, the only pyretic remedy which can be relied on. It should always be a full bath, in as warm a room as can be procured, and should be at a temperature of about 104° when the patient is put into it. The duration of the bath must vary with the circumstances of the case. It should not be less than half an hour, unless the mouth temperature should sooner become normal. During the bath the heat of the water should steadily be increased as fast as it can be borne if the patient be conscious, or if he be unconscious, until a temperature of 108° is reached.

USE OF COLD.

The practical study of the use of cold as a therapeutic measure naturally arranges itself under three divisions: first, its local use; secondly, its very brief general application as a tonic; thirdly, its employment in pyrexia.

LOCAL EMPLOYMENT OF COLD.

When cold is applied persistently to any part, it acts as a direct and very powerful depressant, of varying power according to its intensity. It is, therefore, used locally to reduce *inflammation*, especially when the latter is of an active type. In this employment of cold, care must be exercised not to carry its use too far, lest it suspend all nutritive actions and interfere with those processes of repair which almost always form a part of inflammation. Indeed, it is possible to convert an inflammation into gangrene by the too energetic employment of this agency. Locally, cold is generally applied by means of cold-water compresses, irrigation with cold water and the application of pounded ice, either inclosed in india-rubber bags or in bladders, or in form of the ice-poultice.* It is very doubtful whether the use of "freezing mixtures" is ever justifiable in inflammation. The effects of the cold in individual cases are to be judged of by the alterations in the heat and redness of the part. The local employment of cold belongs, for the most part, within the province of the surgeon, but the remedy is of great value in certain diseases. In *diphtheria* and in *anginose scarlatina*, as originally insisted upon by Dr. Hiram Corson, very great benefit may be obtained by enveloping the throat over the tonsils with powdered ice inclosed in bladders, pieces of pigs' intestines, such as are used by the sausage-makers, or thin india-rubber bags.

In using cold for the purpose of combating inflammation, the application must be kept up until the desired effect is produced. When employed intermittently, cold even becomes a stimulant, the reaction which follows its first impression being greater than its direct effects. Hence the cold douche has been used with asserted advantage as a stimulus to *sluggish ulcers*.

In internal trunkal inflammations, such as *pneumonia* and *pleurisy*, the application of cold wet compresses over the diseased organ has been employed extensively in Germany. In the hospital at Prague every patient suffering from acute pulmonic inflammation is said to be treated with cold compresses, and Smoler affirms that it is very rare that immediate relief is not afforded. Niemeyer states that he has employed the method in a large number of cases of pneumonia with surprisingly good effect, the pain, the dyspnœa, and even the frequency of the pulse being usually reduced in a few hours. On the whole, the evidence in favor of the local use of cold in pneumonia, as well as in the croupous catarrhal pneumonia of children (Bartol, Ziemssen), is so strong, that the repugnance felt to such measures by the profession in the United States would seem to be the offspring of unfounded prejudices.

In *meningitis* the great value of the application of ice to the shaven scalp is undeniable, and in *peritonitis* I have seen very great relief afforded by the use of cold, as recommended by Abercrombie, Niemeyer, and others. As is the case in pneumonia, warm poultices are more generally viewed with favor in peritonitis by the profession in this country. I have frequently used them with excellent effect, and in at least one instance after ice-poultices had been previously employed. In this case the cold applications at first were very agreeable to the patient, as were the warm poultices afterwards, and the good achieved seemed to be in accord with the sensations of the patient. It seems to me a good clinical rule to select the ice or the warm poultice according to the feelings of the patient. Early in the attack, when the fever is high, the ice will generally be the most useful.

Under the head of the local action of cold, it is perhaps proper to allude briefly to the use of the cold douche as a means of reducing *splenic enlargements*. I have had no experience with the measure, but an elaborate experimental and clinical study has led Dr. Fr. Mosler to the following conclusions. In the spleen immediate contact with cold water produces a very perceptible contraction, which is in direct proportion to the coldness of the water; the application of cold water to the abdomen influences similarly but less efficiently the normal spleen; the cold douche applied for two or three minutes, and repeated at longer or shorter intervals, very perceptibly affects the enlarged spleen of intermittent and typhoid fevers, and even of leukæmia. In chronic cases the application should usually be made twice a day (*Virchow's Archiv*, Bd. lvii. p. 1).

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* Made by mixing finely-broken ice with dry Indian meal or fine sawdust.

COLD AS A TONIC AND STIMULANT.

Almost every one has experienced the exhilaration of the reaction which, in a healthy person, follows the sudden dash of a cold shower-bath or the plunge into a mass of cold water. The researches of Liebermeister, which will be detailed hereafter, prove that a cold bath, when of not too long duration, actually increases the oxidation of tissue to such a degree as to elevate the temperature of the body. When cold bathing is employed as a tonic, the first principle to be borne in mind is that the bath should not be too severe or too long continued, else it becomes a direct depressant, debilitating and lowering the temperature of the bather. When the subject has sufficient vital power to react after the bath, sea-bathing is often of very great service, but in debilitated subjects it may produce a serious exhaustion, partly by the fatigue induced, and partly by the excessive abstraction of heat from the body. The cold bath, when not followed by a healthy reaction, is anything but a tonic.

COLD IN PYREXIA.

The use of cold in fever is no new thing: employed by Galen, used not infrequently during the last century, first systematized and insisted upon by Currie, cold bathing in fever was brought before the world as a really new-born measure by Brandt of Stettin, and received the seal of permanent usefulness from the scientific clinical labors of Jürgensen at Kiel.

The consideration of the method naturally divides itself into—first, a study of its physiological action; second, an investigation as to its clinical value; and third, a more particular account of its effect, the cases to which it is best adapted, and the method of its application. Moreover, there are two distinct forms of pyrexia, which may be termed the acute and the chronic, and which are best considered separately.

Acute Pyrexia.—If the following propositions be true, caloric in an excess acts as a direct poison to the body, and the phenomena of severe acute fever are largely due to the heat itself. The proofs of the propositions are given very briefly after them.*

First. External heat applied to the body of the normal animal, so as to elevate the temperature, produces derangement of the nerve-functions, of circulation, etc., precisely similar to those seen in natural fever; the intensity of the disturbance being directly proportionate to the rise in temperature.

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* Want of space prevents the elaboration of this. The unconvinced reader is respectfully referred to the author's treatise on Thermic Fever, and his Toner Lecture on Fever.

Second. Heat applied locally to the brain or to the heart produces in the functions of the organ those disturbances which are familiar phenomena of fever, the intensity of the disturbance being directly proportionate to the excess of heat in the organ.

Third. The withdrawal of the excess of heat in fever is followed by a relief of the nervous and circulatory disturbances.

When a dog, cat, or rabbit is shut up in a box heated either by the sun's rays or by artificial means, the temperature of the animal rises, and at the same time the pulse-rate becomes *pari passu* more rapid, the breathing grows more and more hurried, and the restless, uneasy movements of the victim show the general distress it is suffering. As the temperature increases, the nervous disturbance becomes more and more apparent; and stupor, coma, partial paralysis, convulsions, and finally death by arrest of the respiration, occur. These phenomena sometimes come on gradually, but sometimes are developed suddenly. The temperature at which death occurred in my experiments varied in the rabbit from 111° to 114½° F.; in the dog it was about 111° F. In man a similar series of phenomena are developed by exposure to excessive heat, although, owing to his extraordinary power of cooling his body and of protecting it against cold, he is able to bear extremes of temperature far beyond the points which would prove fatal to any given species of animal. Yet when his body is heated the results are the same, as is proven by the terrible mortality of sunstroke.

To prove the second proposition, I caused hot water to flow through pigs' bladders fitted as a sort of bonnet to the heads of cats and rabbits. It is evident that with small animals we can in this way heat the brain without heating materially the remainder of the body. It was found that coma, with or without convulsions, was produced. Sometimes the stupor came on gradually, hebetude slowly deepening into coma, but in other instances unconsciousness was developed very suddenly. It was found that severe nervous symptoms and death were produced when the brain reached the temperature which was fatal to the animal in the hot box. Without occupying more space, the conjoint labors of Dr. T. Lauder Brunton and of Dr. C. Liebermeister have proven that the accelerated pulse in fever is largely due to the action of the heat upon the heart and its nerves: so that the second proposition may be considered demonstrated.

In regard to the third proposition, I have frequently taken animals out of the hot box perfectly unconscious and plunged them into a bucket of cold water, watched the temperature of the water rise whilst that of the animal fell, and as the bodily heat came towards normal the coma disappeared, so that within ten minutes the at first absolutely comatose and dying rabbit would be skipping about on the grass. I have placed a man whose temperature was nearly 110° F., who was absolutely comatose, with a feeble-running pulse of 160 or 170, irregular, jerking, slow respirations, and every indication of immediate death, in a bath of 60° F., and within a minute and a half have seen consciousness partially restored, and in another minute and a half the man trying to get out of the bath. What could the bath do to affect the man so much but withdraw the heat? That the heat was present and that it was withdrawn the thermometer proved. If the drowsiness had been due to simple congestion of the brain, very certainly would the bath, by driving the blood from the surface, have increased the trouble. It must be borne in mind that this case is by no means unparalleled: similar instances of the good effects of the sudden withdrawal of heat in rheumatic hyperpyrexia have been recorded by both English and German observers, and recent Continental literature is full of reports of the relief of nervous symptoms in various pyrexias by the abstraction of heat.

In conclusion, as excessive heat is present in fever, as excessive heat, when present, not only is able, but is forced, so to speak, by its own attributes, to produce disturbance of the functions of innervation and circulation, and as the withdrawal of the excessive heat in fever is followed by instantaneous relief of the symptoms of disturbed innervation and circulation, surely the conclusion is logically inevitable that excessive temperature is the chief cause of the other symptoms of fever, and that in *acute pyrexia* threatening life the heat should be withdrawn as rapidly as possible by means of the cold bath.

Chronic Pyrexia.—The effects of a long-continued pyrexia, not sufficiently intense to induce immediate serious symptoms, upon the structure of the various tissues, have been elaborately investigated by Liebermeister (*Deutsches Arch. für Klin. Med.*, Bd. i.), who found that the liver, spleen, kidneys, voluntary and involuntary muscles, blood-vessels, and even the nerve-centres, undergo a granular degeneration during a continued pyrexia. The lesion was constantly present in the bodies of those who had suffered in this way during life, entirely independent of the nature of the primary disease. In cases of infectious fever in which the temperature had never been high, this granular degeneration did not exist. Previous to the investigation of Liebermeister, Zenker had demonstrated that the muscles undergo a peculiar granular degeneration in typhoid and other fevers; and the fact has been abundantly attested by later observers. I do not know that the observations of Liebermeister as to the occurrence of this lesion in non-infectious pyrexia have been confirmed, but I have no doubt of their correctness.

It is evident that in all fever a primary therapeutic indication is to reduce the temperature. Of course, if possible, this should be done by checking the excessive production of heat; but, unfortunately, this often lies out of our power, and we are forced to abstract the heat by mechanical means.

It is *a priori* impossible to determine what effect upon the production of heat the rapid abstraction of it would have, but, from the well-known powers of the organism to resist external cold, it seems probable that the heat-production would be increased rather than diminished by the abstraction of caloric. An experimental study of this problem has been made by several observers, but with, unfortunately, different results. Weisflog (*Deutsches Archiv für Klin. Med.*, Bd. ii. p. 570) has found that the local abstraction of heat by a cold sitz-bath causes a rise in the temperature of the axilla, and that in fever-patients, unless the sitz-bath is prolonged over twenty minutes, no fall of the bodily temperature results. In 1860, Kernig (*Reichert's Archiv*, 1860) found that a healthy man in a bath of the temperature of 28° to 30° C. produces about twice as much heat as normal; in baths of 24°, about three times as much; and in baths of 20° C., about four times as much. Liebermeister (*Beobachtungen und Versuche über die Anwendung des kalten Wassers bei fieberhaften Krankheiten*, Leipsic, 1868) found that in a healthy man exposure to cold for a brief period of time causes a rise in the bodily temperature, and on extending his researches into fever proved that where the external cooling was not too powerful or too long continued the same was true of fever-patients. From this it follows that the use of external cold stimulates heat-production. This, to my mind, has been confirmed by the chemical researches upon men of J. Gildemeister (*Virchow's Archiv*, Bd. lii. p. 131), of Dr. L. Lehmann (*Ibid.*, Bd. lviii., 1873), and of Prof. Liebermeister himself (*Deutsches Archiv für Klin. Med.*, Bd. x. p. 89), and by those of A. Roehrig and N. Zuntz (*Pfluger's Archiv*, Bd. iv. p. 66) upon animals, all of which show that both in health and in fever very much more carbonic acid than normal is eliminated under exposure to cold. This would appear to prove that cold baths increase the production of animal heat. It seems most probable that this is the case; but A. Murri believes that he has proven that the cold baths have no such influence.* At any rate, investigations of Liebermeister (*loc cit.*, p. 134) and others have shown that the first rise of temperature produced alike in healthy and in fever subjects by exposure to a moderate and not too long continued cold is followed after removal of the cold by a fall of bodily temperature of greater or less degree. Whilst, therefore, external cold probably first stimulates, it afterwards depresses the production of animal heat. The further experiments of Liebermeister (*Deutsches Archiv*, Bd. x. p. 425) upon the elimination of carbonic acid are also in accord with his temperature-study, for he found that after the bath the elimination sank below normal, and continued so for some considerable time. This conclusion has been strongly corroborated by Dr. N. A. Sassetzky (*Virchow's Archiv*, xciv. 517), who finds as the outcome of an elaborate research that the continuous use of the cold bath lessens invariably the urinary elimination of nitrogenous materials and of the phosphates, although increasing the total flow of urine.

The results of the physiological study of the effects of cold in fever may be summed up as follows. During a prolonged and severe application of cold the bodily temperature falls, although an increased production of heat—*i.e.*, consumption of tissue—probably occurs at first; afterwards the bodily heat continues to fall, or but slowly regains its former position, because there is a diminished production of animal heat with decrease of tissue waste. The increased consumption of tissue which occurs during the cold bath is of no moment, being more than counterbalanced by the lessened production after the bath.

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* I have never seen the brochure of A. Murri (*Del Potere regulatore della Temperatura animale*, Firenze, 1873). It is abstracted in the *London Medical Record*, vol. i.

The clinical evidence in regard to the use of cold in fever may be looked at in two different ways. Thus, we may consider the assertions and results of individual observers who have seen large numbers of cases of fever and used the method faithfully, or we may weigh the sum total of the experience of all who have written upon the subject. At first sight it may appear that the latter is by far the best course to pursue; but it must be borne in mind that the treatment is one opposed to the ordinary medical prejudices, that its efficient carrying out involves so much labor and attention as to be almost impossible to those who disbelieve in its usefulness, and that those physicians who claim most for the method affirm most strongly that to do much good it must be practiced very vigorously and steadily. These things being so, it seems wisest to look at the evidence from both points of view.

M. Franz Glénard affirms (*Glasgow Med. Journ.*, 1874) that there have been from six thousand to eight thousand cases of typhoid fever treated by the use of cold in Austria, Prussia, and Russia, with an average mortality of from four and five-tenths to seven and six-tenths per cent.; the previous mortality under the old expectant method having varied from eighteen to twenty-five per cent. If these figures be correct, they are decisive. Where M. Glénard gets them from, however, I do not know. All the evidence that I have met with is summarized in the following table. Unfortunately, it is not always easy to decide whether a German is writing about typhus or typhoid fever; but where it is not mentioned the probabilities are that the cases are in great part, if not wholly, enteric fever:

TABLE SHOWING THE RESULTS OF THE COLD-WATER TREATMENT IN TYPHUS AND TYPHOID FEVER.

NAME OF REPORTER.	PLACE.	NUMBER OF CASES.	MORTALITY, PER CENT.	REMARKS.
Jürgensen.	Kiel.	160	3.1	Previously 15.4 per cent. Typhoid fever.
Petri.	Lanbbach.	31	3.2	
Liebermeister.	Basel.	1121	8.2	Previously 26 to 30 per cent. Treatment very rigorous. Typhoid fever.
Mosler.	Greifswald.	71	7	
"	"	92	9	Typhus exanthematicus, previously 50 (?) per cent.
Becher.	Ostpreussen.	17	24	Typhus exanthematicus, previously, on an average, 10 per cent.
Brandt.	Stettin.	187	2.1	Private practice.
"	"	84	10	Military Hospital. Previously 30 per cent.
Goden.	"	24	20.8	
Stohr.	Würzburg.	120	6.6	Previously over 20 per cent.
Drasche.	Vienna.	40	10	Year before 16.5 per cent.
Ziemssen.	Erlangen.	32	9.4	Formerly, with bad cases, 30.2 per cent.
Stieler.	Munich.	226	5.6	Formerly 12.15 per cent.

TABLE.—*continued.*

NAME OF REPORTER.	PLACE.	NUMBER OF CASES.	MORTALITY, PER CENT.	REMARKS.
Pastau.	Breslau.	246	11.8	Typhus exanthematicus. Without baths, mortality 16.5 per cent.
Popper.	Prague.	20	5	
Riegel.	Würzburg.	156	4.4	Only serious cases included. Almost every fatal case came in too late for baths to do good.
Götz.	Prague.	54	5.5	Typhoid fever. Other cases treated at the same time, expectantly, 15.4 per cent.
"	"	50	18.8	Typhus exanthematicus.
Scholz.	Bremen.	125	4	Typhoid fever.
Wunderlich.	Leipsic.	155	7	Typhoid fever. Previously 18.1 per cent. out of 1178 cases.
Zaubzer.	Munich.	356	5.6	Typhoid fever. Previously 17.6 per cent. out of 701 cases.
Bauer.	"	87	7	Typhoid fever. Previously 11½ to 16 per cent.
Duchek.	Vienna.	60	28.3	According to Brandt, this high mortality depended upon the treatment having been imperfectly performed.
Krofft-Ebing.	Rastatt.	105	25.7	Only bad cases. Previous mortality 34 per cent.
Wille.	Rheinau.	59	19	
Stecher.	Claye.	146	8.2	
Schönheiden.	Dammartin.	82	3.6	Mild epidemic.
Pfeifer.	Weimar.	58	5.2	
Leube.	Ulm.	47	19	Typhoid fever, among French prisoners of war. Baths of moderate temperature used.
Böhm.	Niederbronn.	131	11.5	Typhoid fever. Military hospital.
Gersauer.	Vigy.	97	6.18	Typhoid fever. Mortality on expectant treatment 23.91 per cent.
Drasche.	Vienna.	55	19	Typhus fever.
Merkel.	Nuremberg.	41	2.2	Typhus fever.
Loebel.	Vienna.	87	18.4	Typhoid fever.
"	"	105	28.6	Typhus fever. The treatment in this and in the preceding case was not thoroughly carried out; the patients mostly receiving only three baths a day.
Glénard.	Lyons.	52	0	Typhoid fever.
Schmidt.	Erlangen.	56	0.18	Several fatal cases not counted, because not received until the fifteenth day, and, therefore, too late to test the treatment; they bring the total mortality to 4.14 per cent.
Heubner.	Leipsic.	72	0.14	
Binz.	Versailles.	190	2.1	Soldiers. Mostly, if not all, typhoid fever.
Zeroni.	Mannheim.	72	18	Soldiers.
Valette.	Lyons.	21	0	Typhoid fever.

This table is of such a character that any lengthy discussion of it seems unnecessary. It is, however, allowable to call attention to the facts that the failure of the method at Vienna is, by the upholders of it, very justly attributed to the inefficient carrying out of it, and that in some other instances the apparent high mortality is due to none but the most serious cases being included, or to the patients having been soldiers, worn out by the hardships and toils of a severe campaign.

When the evidence furnished by single observers is noted, the results are even more astonishing than those of the above table. Jürgensen states that from the year 1850 to 1861 there had been treated in the hospital at Kiel, according to the expectant method, three hundred and thirty typhoid-fever patients, with a mortality of fifteen and four-tenths per cent.; while from 1863 to 1866, during which period the anti-pyretic method was employed in one hundred and sixty cases, the mortality was three and one-tenth per cent. Prof. Liebermeister has employed the cold-water treatment on a larger scale than has any other individual. At the hospital at Basel, up to the year 1865, one thousand seven hundred and eighteen cases of typhoid fever were treated upon the expectant plan, with a mortality of twenty-seven and three-tenths per cent. In 1865, Dr. Liebermeister introduced the use of cold bathing in a timid, inefficient manner, and reduced the mortality, in nine hundred and eighty-two patients treated, to sixteen and two-tenths per cent. In 1866 he commenced the vigorous regular employment of the method, and reduced the death-rate, in one thousand one hundred and twenty-one patients treated, to eight and two-tenths per cent. Prof. Liebermeister himself criticises very closely, in the recent " Encyclopædia of Medicine," these statistics, and raises the mortality, by excluding trifling cases, to from ten to eleven per cent.; but, after the anti-pyretic treatment has been even unjustly dealt with, the statistics still show that the mortality under the cold-water treatment is not half what it formerly was. Further, a certain proportion of cases are always admitted to the hospital moribund, too late for any human agency to be of avail: these cases, of course, maintain the same proportion under any treatment; they really constitute a large part of the deaths seen in the cold-water treatment, so that if they were eliminated from both sides the death-rate " under the anti-pyretic plan would be but a small fraction of what it would be under the other."

In hospital practice the patients are very rarely received upon the first day of the attack, and very frequently do not enter the wards until the third week, so that the statistics, as already intimated, favorable as they are to the new treatment, express only a portion of the truth. If the good effected be so great when the remedy is often not applied until the second or third week, much more is to be expected when it is employed faithfully from the moment the temperature becomes elevated. Accordingly, Brandt is said to claim that if the case be properly treated, from the onset of typhoid fever, death will never occur; and it is stated (*Lancet*, January 23, 1875) that out of two hundred and fifty-nine cases he has had two hundred and fifty-nine recoveries. I have not had access to the original papers of Dr. Brandt, and cannot, therefore, analyze his statistics; but Glénard (*loc. cit.*) is quite as enthusiastic; he states, " You will not find in the five or six thousand cases of typhoid fever treated by this method one single unsuccess among those which have been submitted to it since the beginning of the disease." Prof. Edes, also, states that of thirty-two patients received in the Boston City Hospital during the first week and treated with cold bathing, only one died (*Med. and Surg. Rep.*, Boston City Hospital, 1877). Mayet states that in typhus fever in Lyons, of six hundred and forty-nine treated without cold water, 14.48 per cent. died; of three hundred and thirty-five treated with cold baths, 10.74 per cent. died (*Gaz. Hebdom.*, Mars, 1883).

All those physicians who advocate the use of cold baths in typhoid and typhus fevers appear to be agreed that, although the mortality is very much reduced, the duration of the disease is only shortened in so far as complications are avoided. As, however, the patient is left by the disease much stronger than he is when the expectant method of treatment is pursued, convalescence is much more rapid than under the old plans. By the antipyretic treatment the intense prostration, delirium, stupor, carphologia, involuntary passages, and other manifestations of the typhoid state are greatly lessened. The relief afforded is so evident to both patient and attendants that they usually, after one trial, acquiesce in the regular employment of the cold baths, although to the one the sensations are at first very disagreeable, and for the other the labor and attention required are very much increased. The antipyretic use of cold in typhoid fever has not, however, been free from determined opposition (see discussions in *Le Progrès Méd.*, 1877; also *Bull. Thérap.*, xci.), and the assertions in its favor are some of them evident exaggerations. I am, however, very sure from my own personal experience, as well as from the great mass of evidence now existent, that the method is of the utmost value, and I believe that *the cold bath is safer and more efficient than are antipyretic drugs.*

A very practical question, but one which we are as yet scarcely in a position to answer fully, is, What are the contra-indications to the use of cold in fever? According to our old ways of thinking, bronchitis and pneumonia would especially seem to be in the way. The serious lung-affections of low fevers are, however, largely dependent upon the general adynamia, and this adynamia is, in turn, largely the result of the excessive temperature. Accordingly, the German investigators have not found the baths to do harm in the pneumonias of exanthemata. Liebermeister, who has had more experience than any other man, says that "pneumonia, hypostatic congestion, and the like, offer no reason for suspending the baths; the hypostatic troubles sometimes disappear under their use." I have carried one or two cases, in which the lung symptoms were very severe throughout, to a successful issue, employing cold freely, and was unable to perceive any evil effect upon the lungs. Prof. Raynaud, as the result of his experience, affirms most emphatically that neither pulmonic nor intestinal complications should interfere with the use of the cold bath (*Bull. Thérap.*, xci.). On the other hand, Proust reports (*Ibid.*, xcii.) two cases in which fatal pneumonia of the ordinary type, not the hypostatic pneumonia of advanced fever, was apparently produced by cold baths. Doctor Alix also reports two deaths from pneumonia in three cases in which he tried the baths. My own feeling is that severe bronchitic or pneumonic symptoms occurring in the *beginning* of typhoid fever should make us very cautious in using the antipyretic method, but that when they occur late in the fever, and are due rather to hypostasis than to inflammation, they are not contra-indications to the use of the bath. Prof. Liebermeister affirms that perforation of or hemorrhage from the bowels is a contra-indication to the use of cold in fever, because cold has a tendency to produce determination of blood to the internal organs. The experience of Wunderlich (*Schmidt's Jahrbücher*, Bd. clvi. p. 101) is, however, very much opposed to this idea of Liebermeister's. He treated sixteen cases of severe intestinal hemorrhage with cold baths, with but two deaths; neither of which resulted directly from the hemorrhage, one being from intestinal perforation and one from severe pneumonia. This mortality is certainly a very small one, for when cold water was not employed, out of thirty-two cases Griesinger had ten deaths; out of twenty-one Jenner lost seven: out of fourteen Gietl lost six; and Jaccoud had six deaths in six cases (*Pathologie Interne*, t. ii. p. 758). Bauer, however (*Schmidt's Jahrbücher*, Bd. clvi. p. 101), is in agreement with Liebermeister in believing that the baths should be discontinued during intestinal hemorrhage. Yet their views seem to be based upon preconceived theory rather than upon actual trial. Thus Liebermeister says, "I have thus far ordered the baths entirely discontinued as soon as even slight hemorrhage from the bowels occurred." The proportion of cases in which intestinal hemorrhage occurs does not seem to be increased by the cold-water treatment, at least Golsdammer (*Berlin. Klin. Woch.*, 1877, p. 98) affirms that under the older methods thirteen thousand five hundred and sixty-three cases gave five hundred and thirty of intestinal hemorrhage, whilst five thousand six hundred and thirty-six cases of cold-water treatment yielded two hundred and forty of intestinal hemorrhage, the percentage being in the two cases respectively 3.9 and 4.2. Menstruation appears not to be looked upon as a contra-indication. On the whole, the testimony seems to me to show that no local internal disease ought in the present state of our knowledge to be looked upon as absolutely contra-indicating the use of cold baths when the temperature is high in typhus or typhoid fevers.

It is otherwise when there is a general tendency to collapse,—when the heart is so weak that local stases of blood occur in almost all the internal organs. Under these circumstances the circulation has not sufficient power thoroughly to equalize animal heat, so that it is said to be entirely possible to cool the exterior of the body several degrees without materially affecting the temperature of the interior. One of the severe accidents which it is affirmed has very rarely followed the use of the cold bath in pyrexia is a sudden collapse; and clinical experience seems to indicate very strongly that when collapse is already existent the cold baths should not be administered.

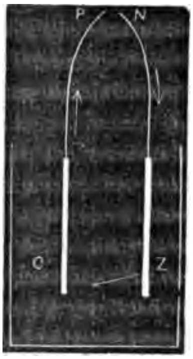
In no disease attended with a long-continued pyrexia has the cold-water treatment been employed upon so grand a scale as in *typhus* and *typhoid fevers*; but the results there obtained are sufficient to indicate its usefulness in allied diseases. Of all the exanthemata, none is more constantly attended with excessive temperature than is *scarlet fever*. In this disorder the testimony to the value of cold is very strong. Going back to Currie, who really first systematized the abstraction of heat in fever, we find that he habitually practiced in the most heroic manner cold affusions in the treatment of scarlet fever, and claimed the greatest success for the measure. Since his day the remedy has been employed with asserted good results by various observers, among whom may be mentioned Gérard, Bruère, Giannini, Armstrong, Laycock, Rilliet and Barthey, Trousseau, and Hiram Corson, of this State. The evidence is, unfortunately, too much generalized to allow of its being put in a statistical form, but for an extended résumé of it the reader is referred to the excellent article in Meigs and Pepper's work on the diseases of children. In almost all of these cases the cold was applied in the form of affusions, a method which is certainly far more terrifying to the child, and probably less efficient, than the cold bath. Recently, Dr. G. Mayer (*Jahrbuch für Kinderkrankheiten*, vii. 4) has been placing the child in a bath of from 93° F. to 73° F. (according to the intensity of the fever) for ten minutes, whenever the temperature rises above 102° F. He affirms that the effect was most beneficial, and that the reduction of temperature usually lasted for several hours. In *diphtheria*, cold bathing has been used to some extent, with seemingly good results. In both this affection and in anginose scarlatina it is of the utmost importance to combine the cold bathing with the local application of the ice-bag or ice-poultice to the throat. During the summer months *serous diarrhœa* (*cholera infantum*), in some of its forms, annually destroys large numbers of children in this country. In most of these cases the bodily temperature is much elevated, and the diarrhœa is produced and maintained by the heat, as originally pointed out by Dr. Comegys (*Philada. Med. Times*, v., p. 665; *Amer. Journ. Med. Sci.*, Oct. 1876). All the ordinary methods of drug administration fail, or, at most, succeed in keeping the child alive until the heat of the weather subsides. Under these circumstances antipyretic treatment acts in a most magical manner. I have always found simple bathing in water at about 75°, at intervals of from three to six hours, sufficient, but in some cases the plan recommended by Dr. Comegys may be required,—namely, by cold affusions whilst the child is sitting in a cold bath. The effect is usually immediate, quiet and sleep at once replacing the wakeful restlessness so distressing to mother and child. There may be a few instances of sudden collapse with low temperature from exhaustion by the serous discharges, but usually cases in which the disease is said to "go to the head," are those in which the temperature rises so high as to produce brain symptoms; under these circumstances the vigorous use of external cold is imperatively demanded.

It is in the highest degree probable that systematic cold bathing will be found serviceable in all blood-poisonings with high temperature, such as smallpox, erysipelas, pyæmia, etc.; but as yet we have no clinical evidence of moment upon the matter. The high temperature that prevails in sthenic *pneumonia* and certain other inflammatory diseases would appear to indicate the abstraction of heat; but how far the local disease will be advantageously or disadvantageously affected in these cases is as yet an open question. Dr. G. Mayer (*Schmidt's Jahrbücher*, Bd. cxlix. p. 347) is stated to have found that defervescence is materially hastened both in men and in children by cold bathing. Dr. Kissler (*Virchow's Archiv*, Bd. xciv. p. 490) had in one epidemic a mortality of 17.4 per cent. in twenty-three cases treated with the cold bath, and of 57.1 per cent. in twenty-one cases treated otherwise. In *dysentery*, Dr. B. Wenzell (*The Doctor*, 1874) strongly advises the use of large enemata of ice-water, which by their local action relieve very greatly the pain and tenesmus, and at the same time have a decided effect upon the pyrexia.

In carrying out the antipyretic treatment of fever certain general considerations should never be forgotten. It should always be remembered that the treatment is directed against a symptom only, and hence is to be used only when that symptom threatens injury. The danger-point may be considered to be a *mouth* temperature of 103°. As it is possible to cool the axilla without cooling the interior of the body, all temperatures should be taken in the mouth or rectum. Again, no bath or other application does good unless it removes the heat, but the cold should never be applied more severely than necessary. I have used cold spongings, cold packings, and the various baths, and have found that when a portable bath-tub can be brought to the bedside of the patient and readily filled and emptied, its use is accompanied with less fatigue and disturbance than any other efficient means of employing cold. The patient, wrapped in a sheet, is to be *lifted* by two attendants into the bath, and then made comfortable with pillows, etc. Unless the pyrexia is very severe, the bath should be at a temperature of 90° F., and cooled down *pro re nata*. When no portable bath-tub is at hand, efficient antipyresis may be had by lifting the patient, wrapped in a sheet, upon a cot covered with a rubber blanket, and sousing rather than sponging him with cold water from a large carriage sponge. If the sacking bottom or the canvas of the cot be so loose as to sag down several inches, and the rubber blanket be turned up at the bottom and top over a wide board nailed across the top and bottom, the patient during the sponging lies in a big pool of water, and all the effect of the cold bath is obtained by removing with a carriage sponge this water as fast as heated, and sousing fresh cold water (ice water if necessary) freely over the upper part of the patient. Under *no circumstances* should the patient be *allowed* to *help himself at all* during the various movements. When the extremities seem especially affected by the bath, they should be rubbed so as to maintain their circulation. I have frequently applied hot-water bottles to the feet whilst the body was being bathed, with good effect.

ELECTRICITY.

FIG. 1.



General Considerations.—Electricity is a force which is developed in various ways, but which is essentially the same entity under all circumstances. When it is obtained by rubbing two surfaces together, it is known as frictional electricity; when by the union of two dissimilar metals, it is called galvanism. Frictional electricity is almost never used in medical practice, and I shall say nothing more about it in this book.

There are a large number of different patterns or arrangements of the elements which generate galvanism, but the ideal or typical cell may be said to be formed of two dissimilar metals immersed in some corrosive liquid and connected with each other by a piece of wire externally. Under these circumstances the current starts from the metal most easily corroded, passing through the liquid to that less easily acted upon, and from this over the external wire to the starting-point. The external end of the least-easily corroded plate is therefore always giving off electricity, and is known as the + or positive pole, whilst the corresponding end of the other plate is constantly receiving electricity, and is spoken of as the — or negative pole. When wires are attached to these plates they become, as it were, prolongations of the plates, and their ends constitute the poles. Thus, in the diagram, $C =$ copper, $Z =$ zinc, P and $N =$ poles, and the arrows show the direction of the current. The positive pole is called the *Anode* (ανω, upwards, ὁδος, a way); the negative, the *Cathode* (κατω, downwards, ὁδος).

As the electric current does not primarily exist, it is evident that in the typical or ideal galvanic cell there must be something which sets it in motion. This force is the so-called electro-motor force, and has been determined by physicists to be a definite quantity for the same combination of metals at the one temperature. This force is generated at the point of contact of the metals, and is in consequence of the law discovered by Volta, that when two metals are in contact with each other a disturbance of the electrical conditions of those metals occurs. The amount and energy of this disturbance vary according to the nature of the metals, and experiments have shown that all metals have definite electro-motor powers or properties, and that they can readily be arranged in a regular series. A study of this series is not necessary to an understanding of electro-therapeutics, and the reader desirous of knowledge upon this especial point is referred to works on physics

It must be borne in mind that the electro-motor force is constant, so that in any given combination of metals in a galvanic cell the electro-motor force is always the same, whether the plates of the metal be large or small, whether the solution be an acid, a saline, or pure water. The strength of the current is not, however, decided entirely by the electro-motor force of the cell. Every known substance refuses more or less imperiously to allow the passage of electricity. The best conductors oppose a really very great resistance. Now, it is evident that this resistance is opposed to the electro-motor force, and that if it be greater than the latter it will altogether prevent the passage of any current. The strength of the current, then, depends upon the relation between the resistance and the electro-motor force; and we have the celebrated law of Ohm, which may be expressed by the formula $c\ (\textit{current-strength}) = \frac{e\ (\textit{electro-motor force})}{r\ (\textit{resistance})}$. This law experiment has shown to be imperative: no increase or diminution of the size of the plates, no change in the character of the solution, affecting it.

The resistance to the current in a galvanic combination is a double one: inside of the cell the fluid between the plates opposes the passage of the electricity, and outside of the cell the conductor which completes the circuit also offers a resistance. The reason a battery almost ceases to yield a current when water is substituted for the acid usually employed is not a purely chemical one, but simply because water is an almost complete non-conductor, and offers triumphant resistance to the current, whilst the acid conducts and readily allows the current to pass. The entire resistance (r) is then made up of two factors: the internal resistance (ir), and the external resistance (er). The formula of Ohm may therefore be read $c = \frac{e}{ir + er}$.

As already stated, when the plates of a cell are increased in size the electro-motor force is not increased, but as the surfaces of the plates are increased the diameter of the conductor—*i.e.*, the mass of fluids between the plates—is increased; and consequently, as the resistance in a conductor is inversely as the size of its cross-section, the strength of the current is increased. To make this a little clearer, suppose ir in a certain cell equal 10, then $c = \frac{e}{10 + er}$: if now the plates of the cell be doubled in size, $c = \frac{e}{\frac{10}{2} + er} = \frac{e}{5 + er}$. A similar result—*i.e.*, lessening of the internal resistance—can be achieved by shortening the distance between the plates of the cell,—*i.e.*, the length of the conductor,—or by in any way making the intervening liquid a better conductor.

The change in strength of a current by the increase of the size of the plates of the cells can readily be expressed by the formula of Ohm. If the letters signify as before, and the internal resistance be diminished y

times by increasing the size of the plate y times, instead of $c = \frac{e}{ir + er}$ c will $= \frac{e}{\frac{ir}{y} + er}$. If, instead of a single cell, a number of cells are arranged in such a way that the copper of one is connected with the zinc of the next, the electro-motor force of the combination is equal to the sum of the electro-motor forces of the cell: thus, if $e =$ the electro-motor force of the single cell, and $y =$ the number of cells, the electro-motor force of the battery will be ye. It is also plain that the internal resistance of the battery is also increased y times, so that the formula of Ohm will stand $c = \frac{ye}{yir + er}$.

Of course, the strength of a current is greatly affected by the external resistance. In very many instances the external resistance is enormous. Suppose, then, this external resistance in a given case be 1000 times the internal resistance, the formula of Ohm will read, $c = \frac{e}{ir + 1000\,ir}$. It is evident that under these circumstances ir, the internal resistance, becomes very insignificant, and that very little is gained by increasing the size of the plates,—*i.e.*, by diminishing the internal resistance; for if the plates were increased fivefold, the increase of the strength of the current would only be the difference between $\frac{e}{\frac{ir}{5} + 1000\,ir}$ and $\frac{e}{ir + 1000\,ir}$, a difference which is very slight. On the other hand, when the external resistance is very great, everything is gained by increasing the number of cells,—*i.e.*, increasing the electro-motor power; for $\frac{5e}{5\,ir + 1000\,ir}$ gives a very different result from $\frac{e}{ir + 1000\,ir}$. *When, therefore, the external resistance is many times greater than the internal, practically nothing is gained by increasing the size of the plates; everything by increasing the number of the elements.*

The converse of the above reasoning also holds. If the external resistance be very slight, the internal rises in importance. Thus, suppose $er = \frac{ir}{1000}$. Then the formula would be $c = \frac{e}{ir + \frac{ir}{1000}}$. In this case a great deal is gained by increasing the size of the plates, for $\frac{e}{\frac{ir}{5} + \frac{ir}{1000}}$ gives a very different result from $\frac{e}{ir + \frac{ir}{1000}}$. In such a case, by quintupling the size of the plates the strength of the current is practically increased fivefold. On the other hand, it is plain that when the external resistance is slight the gain by increasing the number of cells is a slight one, for the internal resistance is increased as many times as the electro-motor force. Thus, if five cells are used, the formula will be $c = \dfrac{5\,e}{5\,ir + \dfrac{ir}{1000}}$, which will, of course, give practically the same result as $\dfrac{e}{ir + \dfrac{ir}{1000}}$.

The law, then, may be stated to be that when the *external resistance is very slight, increasing the number of the elements has no practical effect upon the strength of the current, whilst an increase of the size of the elements has the greatest effect.*

When there is no very *great disproportion between the internal and the external resistance, it is evident that the strength of the current may be increased either by increasing the size or the number of the elements.* Thus, if $er = ir$, $c = \dfrac{e}{ir + er} = \dfrac{e}{ir + ir}$; and increasing the size of the plates fourfold will give the formula $c = \dfrac{e}{\dfrac{ir}{4} + ir}$; or increasing the number of the elements to four will yield the formula $c = \dfrac{4\,e}{4\,ir + ir}$. Perhaps the result will be clearer if figures be used. Suppose $e = 100$, $ir = 10$, and $er = 10$. Then the first formula will be $c = \dfrac{100}{10 + 10} = 5$; the second, $c = \dfrac{100}{\dfrac{10}{4} + 10} = 8$; the third, $c = \dfrac{400}{40 + 10} = 8$. When, therefore, the *external and the internal resistance are equally balanced, the strength of the current is equally increased by increasing the number or the size of the plates.*

The application of the foregoing principles to electro-therapeutics is a very simple one. In the ordinary applications of electricity to the body, the resistance of the tissues is very many times greater than the internal resistance of any battery, and consequently the latter may be totally disregarded. Hence for ordinary purposes the formula stands $c = \dfrac{e}{er}$, and power can be gained only by increasing e,—that is, by augmenting the number of cells.

When, however, it is desired to act upon the blood in an aneurismal sac, the needles are brought close to each other; and, moreover, the blood is a comparatively good conductor of electricity. Hence in such cases the external resistance is so much reduced that the internal becomes of such importance that it should not be overlooked. It follows, therefore, that when an aneurism is to be acted upon the plates should be increased in size, whilst at the same time a number of cells should be used.

In the so-called "galvano-cautery" the current is not passed through the body at all, but through a wire, which is thus kept at a white heat. In this case the external resistance is vastly less than when human tissues form a part of the circuit. Hence it becomes a matter of importance to reduce to as great a degree as possible the internal resistance, and the elements or plates should be very large and should be placed very close to one another in the cells. The external resistance is not, however, so slight that it can be entirely overlooked, and hence a number of cells are combined with one another, so as to give sufficient electro-motor force.

In writing or speaking about the use of electricity in medicine, it is a matter of great importance to avoid the use of the old terms *quantity* and *intensity*, which, to use the language of one of the most eminent of living writers on galvanism, "are remnants of an erroneous theory." The amount of mystification which has been produced by talk concerning the therapeutic effects of currents of large quantity with low intensity as contrasted with those of currents of high intensity and low quantity is equalled only by the amount of nonsense which has been written. Currents of galvanism have really only one attribute,—*i.e.*, current-strength,—and that is in strict obedience with the law of Ohm.

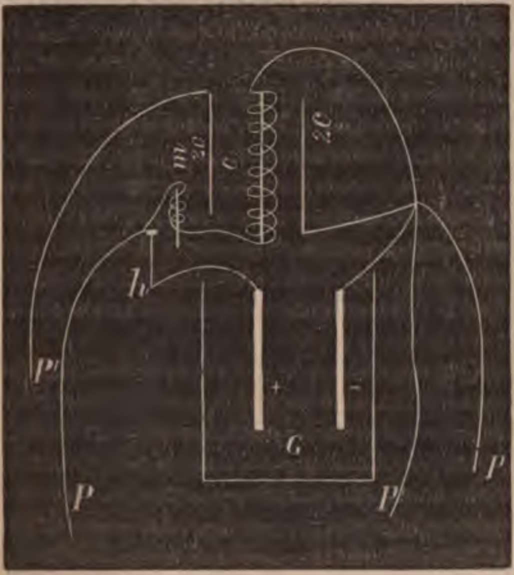
Again, a dense fog has been thrown around the subject of electro-therapeutics by the idea that there are various essentially different forms of galvanism. The current which flows from a cell or a combination of cells is spoken of as a *continuous current*, or sometimes as a *primary current;* besides this, modern therapeutists use another series of currents, which are known as the *induced currents.*

The term *primary current* is often applied to one of these induced currents. If we employ the name *continuous current* for that current derived from the galvanic cell, we must continually be speaking of the interrupted continuous current, which certainly is inelegant. I shall, therefore, employ the name *chemical current* or *galvanic current* to designate that form of galvanism which is generated in the galvanic cell.

If a coil of insulated wire have a bar of soft iron placed in its centre and be surrounded by an external coil of wire, when a chemical current is passed through the first coil, owing to physical laws which it is not necessary here to consider, every time the galvanic circuit is completed or interrupted a brief current of electricity is induced in the inner or first coil, and also a similar current in the outer or second coil. The only physical facts which it is necessary for us to know are that these induced currents are very brief and of great strength, also that they are to-and-fro currents,—that is, run in opposite directions in each individual coil. Thus, in the inner or first coil, when the galvanic circuit is closed, the induced current in the inner coil runs parallel to the generator chemical current, but when this current is broken, the induced runs in a contrary direction. In the outer coil, the induced current, which is instantaneously developed when the galvanic current is sent through the inner coil, pursues a direction opposite to that of the chemical current; but when the latter is broken, the return induced current in the outer coil runs parallel to the generator current.

As these induced currents run backwards and forwards, to and fro, in this way, it would appear that there could not be any negative or positive pole to the battery which generates them, for if one end or pole of the wire constituting the coil be negative in regard to the first induced current, it must be positive in regard to the second or return current. This is assuredly true so far as concerns the outer or second coil, but is not true for the inner or first coil, as is readily understood by means of this diagram of an induction battery.

FIG. 2.



G Galvanic element, with the + and — metals in it.
c Coil in which the primary induced current or currents of the first coil are generated.
h Spring-hammer or vibrator.
m A piece of soft iron becoming a magnet when the current is passing.
2c Outer coil in which the secondary induced current, or current of the second coil, is generated
P Handles of inner coil.
P' Handles of outer coil.

It is plain that when the current is passing, the hammer *h* being in the position represented in the diagram, *m* will become magnetic and attract *h*. This at once breaks the current, and an induced current runs through the first coil and is received by the patient grasping the handles *P P*. The instant the current is interrupted, *m* loses its magnetism and the spring-hammer flies back. Now the circuit is closed, and for the second time an induced current runs through the first coil *c*. It is evident, however, that this induced current of closure will not pass through the body of the person grasping the handles *P P*, but will pass along *h* through the cell to the other end of the coil, as a shorter route and one of vastly less resistance. It is plain that from the inner or first coil the induced current of broken circuit alone passes through the body of the patient.

In regard to the outer coil, it is evident that when the circuit is closed the momentary induced current must run through the body of him who grasps the handles *P'* and *P'*, and that the return current which passes when the circuit is broken must take the same route.

It follows from the above considerations that the *current of the first coil* runs through the patient *only in one direction*, and electricians may correctly mark poles + and —; but that the *current of the second coil* runs in *both directions*, so that any designation of its handles as positive and negative is incorrect. The only justification for the marking of the secondary or outer current poles, as is often done, is found in the fact that the induced current of the broken circuit is stronger than that of the closed circuit. Hence it is that with very strong currents the two poles can sometimes be distinguished when grasped in the hand. The difference is, however, a slight one, and for all practical purposes the induced current of the outer coil is a to-and-fro one, without any negative or positive poles.

If a strong continuous galvanic current be passed through a person, a shock is felt at the moment of making and breaking the circuit, but whilst the current is passing no sensation is perceived except at the points of entrance and exit. Or if the current be passed through the nerve of a muscle, that muscle violently contracts at the moment the circuit is made or broken, but whilst the current is flowing is quiescent. If a rapidly interrupted faradic current be passed through a nerve, the muscle supplied by that nerve is thrown into a continuous spasm. The reason of this is obvious. The so-called faradic or induced current is, as has already been stated, a succession of instantaneous broken currents for the first coil, and as brief to-and-fro currents for the outer coil; so that the circuit is continually being closed and broken, and the muscle is continually excited to action. There is, therefore, a different result achieved in the application of the continuous and induced currents, not because there is any real difference in their nature, but because the mode of application is diverse.

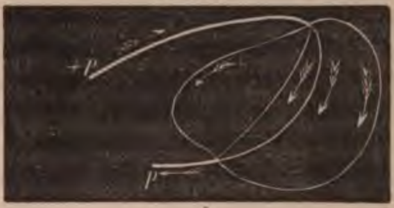
Most medical electricians teach that the true galvanic current is very different from the faradic current, and many, like Duchenne, persist in asserting that the currents of the first coil are essentially different from those of the second. Galvanism is, however, galvanism; and its nature and attributes are probably always the same; the faradic currents are lacking in the chemical power of the continuous current because they pass so quickly that they have not time to exert a chemical influence. Gunpowder can be passed so quickly through the hottest flame as not to ignite it. The secondary induced current differs somewhat in its action from the primary simply because the latter is not a to-and-fro current, and we cannot readily convert an induced into a galvanic or chemical current, because we cannot readily tie together, as it were, the ends of the brief currents into one. I have no doubt that if we could get the interruptions at the rate of many thousand times a minute, we should find that the primary induced current would act as a continuous current.*

We can readily, by mechanical means and contrivances, interrupt the continuous current, or even rapidly reverse the poles so as to give a to-and-fro current like that of the outer coil. When this is done, it is impossible to distinguish between the action of the galvanic and that of the faradic current in producing muscular contractions. It is true that in certain diseased states of the muscle it has been asserted, and with apparent reason, that the action of the induced current is essentially different from that of the true galvanic current. But I believe further investigation will show that the seeming differences are really due to the difference in the lengths of time during which the currents are passing, and not to any inherent peculiarities of the various currents themselves.

It is of the utmost importance to determine by what route or routes galvanic currents pass through the body when the poles are applied to it, and, since the body as a galvanic conductor is governed by ordinary physical laws, some knowledge of these laws is a necessity to the electro-therapeutist.

If a current be passing along a homogeneous conductor, such as a wire of iron, of copper, or of other metal, and that conductor splits up into a number of branches, the current also divides, as is illustrated in the diagram (Fig. 3). If these branches, being of equal size and length, offer an equal resistance, the current divides equally; but if the size or length, and consequently the resistance, of the branches be unequal, the division of the current is unequal; the law being that the strength of the current in each branch of the conductor is inversely proportional to the resistance of that branch. This law is as applicable to conductors composed of

FIG. 3.



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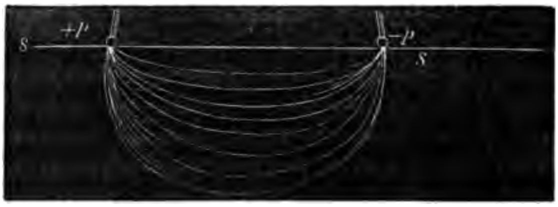
* It has been found that when a faradic machine, or its equivalent, the so-called magneto-galvanic machine, is so constructed that the interruptions are excessively rapid and the to-and-fro currents separate from one another, the infinitely rapid succession of instantaneous induced currents in one direction has all the chemical effects of a steady current; in other words, the interruptions are so brief that they are without influence. I am not aware of any trials with these machines upon living tissues, but do not doubt that their currents will be found to produce the same results as chemical currents.

many substances as to those composed of a single substance; but then the resistance in a branch depends upon the specific resistance of the substance of which it is composed, as well as upon its size and length.

In applying these laws to the passage of galvanism through the body, it must be borne in mind that the dry skin offers an enormous resistance to the passage of the current, so that practically none of the latter will pass *along* it. On the other hand, when the skin is thoroughly wet with salt water it allows the current to pass *through it* readily.

Let us suppose, then, that in the diagram (Fig. 4) $+p$ and $-p =$ wetted poles; *ss* = skin, with the tissues below it. It is evident that, if the tissues were a uniform mass, the current, passing through the skin as a solid bolt, would break up into an infinite number of curved currents, which would meet and pass through the skin again as a solid mass at $-p$. It is equally plain that, of these sub-currents, those whose course was nearest the straight line from $+p$ to $-p$ would be the shortest, and would, therefore, meeting with the least resistance, be the strongest, whilst as the curve and consequently the length and the resistance increased, the strength of the current would diminish until it became practically null. In this imaginary case, the tissue beneath the skin has been supposed to be homogeneous: in actual life the tissue never is homogeneous, and the resistance of the different constituents varies somewhat. Consequently, the strength of the subdivisions of the current is modified: those branch streams being increased which run along or through tissues that conduct readily, and *vice versa*.

FIG. 4.

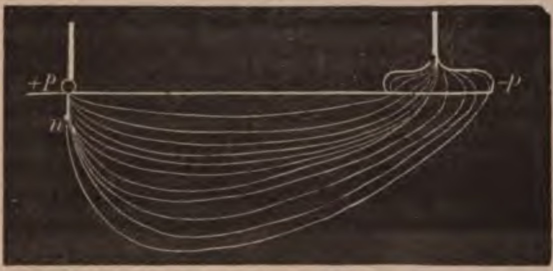


By remembering these facts, we are enabled to apply electricity as closely as may be to any desired portions of the body. Thus, if it be intended to affect as exclusively as possible a certain spot or minute portion of a nerve, a well-wetted small electrode is placed directly over this portion, and, especially if the nerve be somewhat deeply situated, pressed down firmly, so as to condense the tissues as far as possible into a homogeneous mass, whilst a large wet electrode is placed at a small distance from it in a situation which the anatomy of the part will readily suggest. The diagram (Fig. 5) will perhaps illustrate this point more clearly than would many words.

It is evident that the spot immediately under the small electrode will receive the full strength of the current, which is directly afterwards so broken up as to affect very slightly any other part.

Again, suppose it is desired to pass a current through some length of a nerve; it is evident, in the first place, that two small electrodes should be chosen, and that they should be well wetted and pressed firmly upon the trunk of the nerve at the two ends of that portion which is to be affected. Again, in applying electric currents to muscles it is found that if the currents be sent through the body of the muscles, only very imperfect and partial contractions occur, unless indeed the currents be excessively strong. Duchenne was the first to discover that when one pole is placed over certain spots or points in the muscle, violent general spasms of the muscle are produced by currents usually too feeble to elicit a distinct response. To these places the name of *motor points* has been given. These motor points correspond to the position at which the supplying nerve enters the muscle. When it is desirable to affect chiefly or solely a given motor point, it is evident that one small well-wetted electrode should be pressed firmly over the motor point, and another large sponge electrode placed at some little distance from it, in the manner which has already been explained.

FIG. 5.



For certain purposes, to be hereafter explained, it is often desirable to affect chiefly the skin by the electric current. Under these circumstances the skin should be well dried. It then offers so great a resistance that only currents of considerable strength are able to force their way through, and even these currents, taking advantage of the natural apertures formed by the sweat- and other glands, are broken up into a number of branch currents. The galvanic current reaches the internal structures in a great number of small streams very much reduced in power by the resistance they have overcome. If the second pole of the battery be a large well-wetted disk or sponge at a distant part of the body, it is evident that these branch currents will separate and subdivide in such a way that their effect upon the deeper structures will be almost entirely lost.

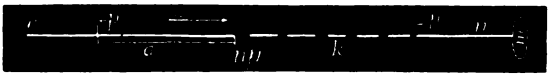
It is a principle in physics that electricity upon points does not strictly obey Ohm's law, but the force accumulates on the extreme end of the point until its density is excessive, and until its self-repulse power becomes so great as to break down all resistance, and to break off highly electrified particles of the conductor, which fly off through the air. It is this which renders the so-called "*electric brush*" so energetic in its action on the skin. This instrument consists of a number of wires united in the form of a cylindrical brush and connected with one pole of the battery; when this is brought in contact with the skin of a person, on whom at some distance is placed the other large well-wetted electrode, each wire point offers a dense accumulation of electricity, which forces its way at all hazards through a minute portion of the skin. The whole current of course enters the deeper tissue in an infinite number of subdivisions, and consequently its effect in these tissues is reduced to a minimum.

PHYSIOLOGICAL ACTION.—When a moderately strong current of galvanism is passed along a certain length or portion of a nerve, there appear between the two poles two zones of disturbed nerve-function, separated by a neutral point at which the nerve retains its normal condition. In the neighborhood of the positive pole the irritability of the nerve, and also its power of transmitting impulses, are diminished, whilst in the proximity of the negative pole these nerve-attributes are increased: to the condition of diminished activity the name of *analectronous* has been applied, whilst that of increased activity has been called *katalectronous*. Thus, in Fig. 6, *cn* equals the nerve; $+p$ and $—p$, the positive and negative poles respectively; *np*, the point at which the function of the nerve remains normal, with the zone of analectronous (*a*) on the one side, and that of katalectronous (*k*) on the other. The longer the current continues, and the more intense it is, the more does the zone of analectronous gain upon that of katalectronous, or, in other words, the more closely does the neutral point (*np*) approach the negative pole ($—p$). Consequently, when a strong current has passed for a length of time through a nerve, the zone of katalectronous is a very short one, confined to the immediate vicinity of the negative pole.

When the particles of a motor nerve pass from a state of inertia to one of motility,—*i.e.*, from one of diminished to one of increased excitability,—the nerve is momentarily excited, and gives origin to an impulse. Therefore, when analectronous disappears in a nerve,—*i.e.*, when a condition of diminished activity becomes one of normal activity,—an impulse is generated just as certainly as when katalectronous—*i.e.*, increased functional activity—appears in a nerve previously normal.

Suppose (Fig. 6) *cn* represents a nerve, and *m* the muscle to which it is distributed. If, then, a downward current be applied to this nerve, it is plain, $+p$ being the positive pole and $—p$ the negative, that *a* will be the zone of analectronous, *np* the neutral point, and *k* the zone of katalectronous. When the circuit is closed in obedience to the law already enunciated, an

FIG. 6.



impulse starts from *k*, and, in order to reach *m*, has to pass only through the stretch of normal nerve between —*p* and *m*. Therefore this impulse of circuit-closure reaches the muscle unimpaired.

Again, when the circuit is broken, the impulse which is generated in *a*, in order to reach the muscle travels only through the zone *k*, whose conducting-power is increased, and a portion of normal nerve; consequently it also reaches the muscle unimpaired. It is plain, then, that with *descending currents strong movements must be induced, both at the making and at the breaking* of the circuit.

With *ascending currents* the results are different. Thus, in Fig. 7, *cn* = nerve; *m* = muscle; +*p* = positive pole; —*p* = negative pole; *np* = neutral point; *a* = zone of analectronous; *k* = zone of katalectronous. Now, it is plain that the impulse generated in *k* at the closing of the circuit must pass through *a*, the zone of diminished conducting-power, in order to reach *m*. Consequently, with the ascending current the contractions of circuit-closure are very feeble, or are altogether wanting. When, however, the circuit is broken, the impulse generated in *a* reaches the muscle *m* unimpaired.

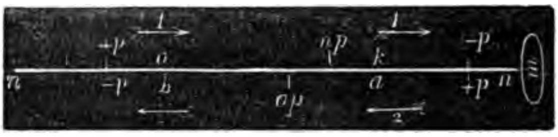
FIG. 7.

Without occupying more space with a discussion of the subject of electrotonous, but contenting myself with the statement that these facts and reasonings apply especially to such currents of moderate strength as are with propriety employed in therapeutics, it is plain that descending currents ought to be more efficient in inducing contractions than are ascending currents. What science thus has discovered, clinical medicine has also found out: descending currents are in practice found to be more powerful than ascending currents.

From what has been already said, it is so evident as scarcely to need further demonstration that the breaking of a current running in one direction must render the nerve more sensitive to the closure of a current running in the opposite direction, but less sensitive to the closure of a current running in the same direction; for when the currents pass in opposite directions analectronous suddenly becomes katalectronous,—*i.e.*, that which was below normal suddenly becomes above normal,—whilst with parallel currents analectronous remains analectronous.

To make this more clear, however, Fig. 8 may be employed. In it the letters have the same significance as in those previously used, whilst the arrows on the side of the lettering represent the direction of the current to which the lettering applies. The downward current is supposed to be broken, and to be followed instantly by the upward: of course the upper, *a*, changes into *k*, and a doubly powerful impulse is sent down to *m*. Now the upward current is broken, and the downward sent through the nerve; at once the lower *a* becomes *k*, and *m* receives again a doubly powerful impulse.

FIG. 8.



The practical application of this reasoning is a very apt one. It becomes, in the first place, very plain why the secondary to-and-fro current of the induction coil has so much more power over muscles than has the primary induced current or the chemical current, as ordinarily applied.

If, however, instead of the chemical current being simply interrupted, its polarity be suddenly reversed at brief intervals, all the effects of the to-and-fro induction current upon healthy muscle are obtained. More than this, for reasons to be hereafter adduced, in certain muscular paralyses I have found that muscles which fail to respond to all other currents respond readily to a very slow to-and-fro chemical current.

Having obtained an idea of the manner in which galvanic currents produce muscular contraction, it is next in order to study their influence upon diseased muscles.

If a muscle by destruction of its supplying nerve be cut off from all spinal influence, it or its nerve rapidly undergoes a degeneration.* In the course of a very few days it will be found upon testing that the muscle no longer responds to a rapidly-interrupted faradic current, but does respond to such current when slowly interrupted; a couple of days later, and the muscle fails to contract to the most powerful and most slowly-interrupted induced currents. When, however, the continued current is applied, and is very slowly interrupted, or, better still, reversed at intervals of one or two seconds, contractions are produced. It is this fact which has led to the belief that there is some intrinsic and inscrutable difference between the induced and the chemical currents. But time is an element required for the propagation of any force. If the hand be passed rapidly through a flame, the latter is not felt; if the hand move more slowly, a sensation of warmth is perceived; if the motion be still slower, this sensation becomes pain. Now, if the hand be partially anæsthetic from disease, in order for the sensation of warmth to be perceived motion must be much slower than in the first instance. In other words, more time is required for the partially paralyzed sensory nerve to perceive heat than for the normal nerve to do so. What is true of the sensory nerve is true also of the motor nerve. It does not respond so quickly to stimuli when partially paralyzed as when normal. The muscle first loses its power of responding to those galvanic currents which are excessively rapid, then to those which are less so, and finally to all induced currents, because from their very nature these currents, even when slowest, last but a fraction of a second. The chemical current may be continued for any length of time at the will of the operator, who is thus enabled to act upon a muscle whose nerve has become so insensitive that it fails to perceive the flash of faradic galvanism.

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* The peculiar electrical reactions of a degenerating muscle are given in detail on p. 695.

The proof of this somewhat dogmatic reasoning is to be found in the fact that the rapidly-interrupted chemical current is no more able to affect the diseased muscle than is the rapidly-interrupted faradic current, as I have proven over and over again in various forms of paralysis. That there is no difference between the chemical and the induced currents in their chemical action, excepting in so far as their influence is affected by the duration of their passage and the to-and-fro character of many induced currents, is abundantly proven by the "Gramme magneto-electric machines," in which an induced current is obtained with almost infinitely rapid interruptions and running only in one direction. With this current all the phenomena of chemical decomposition, etc., are obtained, and no doubt the effects of the continued chemical current upon the human frame would be producible.

THERAPEUTIC APPLICATION.—*Motor System.*—Galvanic currents are employed in paralytic affections for three distinct purposes,—namely, *diagnosis*, *prognosis*, and *therapeusis*. These I shall consider in the order in which they have been enunciated.

There are certain palsies, such as pseudo-muscular hypertrophy, in which the muscular structure is so destroyed independently of any involvement of the nervous system that no response to the galvanic current is possible. All of these palsies are, however, essentially exceedingly chronic, and their diagnosis is to be made out chiefly by a microscopical examination of the muscles themselves. As electricity does not come into play in the diagnosis of these cases, I shall not say more about them. It is otherwise with suddenly-developed paralysis in which the history does not point to any immediate cause, such as diphtheria. Often, in such cases, galvanism is of great diagnostic value. As stated previously, when a muscle is entirely deprived of the influence of the spinal centres it rapidly loses its electro-contractility, whereas, if a muscle be paralyzed from a lesion of such character or position as not to interfere between it and the trophic cells of the cord, it maintains its integrity for many weeks. When a muscle is degenerating for want of spinal influence, it first loses its power of responding to rapidly-interrupted faradic or chemical currents, then to slowly-interrupted faradic currents, then to slowly-interrupted chemical currents, and lastly to slowly-reversed chemical currents. At this time occurs with the galvanic current the so-called "*reaction of degeneration*," first discovered by Brenner, and since elaborated by Erb (*Ziemssen's Encyc.*, xi. 273) and G. B. Massey (*Med. News*, Feb. 1883, p. 124). To comprehend this, it must be remembered that it is obtainable only by applying the electrode to the muscle: if the electrode be applied to a nerve-trunk of a degenerating muscle it will be found that reaction is diminished in quantity but not altered in quality. When a galvanic current of only moderate strength is used, and the negative pole (kathode) placed over the normal muscle but not over its motor point, a strong contraction occurs at the closure of the circuit; when, however, the positive pole (anode) is placed over the normal muscle the contraction is much less; in neither case is there any contraction when the circuit is broken: in other words, with the normal muscle and a feeble current we obtain good kathodal closing contraction, slight anodal closing contraction, and no motion whatever at either kathodal opening or anodal opening. When a current of sufficient power is used, opening contractions are produced, and the anodal contraction is greater than the kathodal. The "reaction of degeneration" consists merely in a more or less perfect reversal of the above formula. The anodal (positive pole) closure then causes a stronger contraction than the kathodal (negative pole) closure. When there is only a slight degree of degeneration present, there is a correspondingly slight increase of anodal closing over kathodal closing contraction. A minimum degeneration would be indicated by an equality of the two closing contractions.

These alterations in the electrical relations of a degenerating muscle are readily formulated, and in this way are perhaps more readily grasped by the student. The symbols are as follows: An Cl C represents *anodal closing contraction;* An O C represents *anodal opening contraction;* K Cl C represents *cathodal closing contraction;* K O C represents *cathodal opening contraction;* $<$ represents *is less than;* $>$ represents *is more than* (the point of the $<$ being towards the lesser quantity). Then the formulas are:

$$\left.\begin{array}{l}\text{An Cl C} < \text{Ca Cl C}\\ \text{An O C} > \text{Ca O C}\end{array}\right\}\text{muscle normal.}$$

$$\left.\begin{array}{l}\text{An Cl C} = \text{Ca Cl C}\\ \text{An O C} = \text{Ca Cl C}\end{array}\right\}\text{muscle in first stage of degeneration.}$$

$$\left.\begin{array}{l}\text{An Cl C} > \text{Ca Cl C}\\ \text{An O C} < \text{Ca O C}\end{array}\right\}\text{muscle in more advanced stage of degeneration.}$$

After the latter Reactions of Degeneration (De R of some authors) have been established, if the muscle continue to undergo change, the galvanic irritability slowly diminishes, stronger and stronger currents being required to produce an effect. When a certain stage is reached all reactions cease, save a feeble An Cl C, and at last this is lost, and the muscle responds not at all. When recovery occurs, the electrical reactions of the muscle pass upwards along the pathway they have descended.

The practical importance of the Reactions of Degeneration is greatly lessened by the circumstance that their demonstration usually requires much skill and patience,* and that it probably is never present when a muscle still retains its integrity as regards the faradic current. For the purposes of the practitioner, the failure of response to the latter current is the best test as to the condition of a muscle. When a muscle loses its power of responding to the rapidly-interrupted faradic current in a week or ten days after the occurrence of paralysis, whether the reaction of degeneration can or cannot be satisfactorily demonstrated, the inference is very positive that the lesion either is one of the nerve-trunk, or, if of a nerve-centre, is of such a character as seriously to involve the trophic cells of the spinal cord. If a few days later such muscle is unable to respond to any faradic current, this inference becomes a certainty. Under these circumstances, the possible lesion is narrowed down to infantile paralysis, a conceivable destructive myelitis, and an affection of a nerve-trunk.

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* Dr. Massey gives the following directions as to the method of making the test: "Having placed one well-moistened electrode over the muscle to be tested, and the other

A *myelitis* so rapid and severe as to destroy in a few days a portion of the spinal cord, and consequently the electro-contractility of its tributary muscles, is exceedingly rare, and, if it occurred, could only be confounded with spinal congestion complicated with hemorrhage. In *infantile palsy* the nature of the case is usually but too apparent, although the muscles often lose their electro-contractility as quickly as when a nerve-trunk is severed. Practically, therefore, very rarely is there any difficulty in recognizing the seat of the lesion in acute organic palsies by means of the galvanic test. It may be laid down as a practical rule *that when in the adult a muscle loses to a sensible degree in a few days its electro-contractility, the lesion is in a nerve-trunk.* In recognizing, however, these peripheral palsies, it must not be forgotten that the injury to the nerve may be very deeply situated,—even within the membranes or substance of the nerve-centres. This is especially to be borne in mind when it is a cerebral nerve that is affected. Thus, a tumor situated in a superficial portion of the brain may press upon the fibres of a nerve just as they are collecting together previous to leaving the brain, and the result will be a palsy which is really a peripheral one, although the tumor is in the nerve-centre. A similar thing may happen to the spinal cord: thus, I have seen, in spinal congestion giving origin to meningeal apoplexy, *rapid* and total destruction of the electro-muscular contractility in the lower extremities, from the pressure of the clots upon the cauda equina.

The persistence of the muscular contractility intact for some weeks after

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in some carefully-selected point of departure, it next becomes necessary to properly close and open the circuit. For this purpose nothing is in any way comparable to a pedal rheotome, a simple mechanism worked by the foot; it is, in fact, a necessity whenever the services of an assistant cannot be obtained, as a steady application of the electrodes is essential in many delicate cases,—even the slightest movement produced by the working of the hand-current-breaker being confusing. If the pedal rheotome also contains a commutator, worked by the foot, for changing the poles while still *in situ*, its handiness will be greatly increased. The clock-work current-breakers usually furnished by instrument-makers are totally unfit for diagnostic purposes."

the occurrence of a palsy depending upon an organic lesion, proves that the disease is of cerebral origin, or, being spinal, is of such nature as not to compromise seriously the trophic nerves of the cord.

In applying these rules, it must not be forgotten that whenever a muscle is not used it loses its contractile power, so that even in paralysis from cerebral hemorrhages the muscles finally degenerate, although this degeneration is rarely so complete as in peripheral palsies. It is not the fact of degeneration, but its degree, and especially the period of time which elapses between its occurrence and the commencement of the paralysis, which is the important factor in the diagnosis. In cerebral palsies no distinct loss of functional activity in the muscles is usually perceived sooner than six weeks after the onset of the attack, and even after years have elapsed some response may often be elicited by strong slowly-interrupted or reversed currents.

There are certain palsies in which the electro-muscular contractility is really or apparently above normal. Very frequently the excessive contractions produced are not so markedly in the muscles to which the currents are applied as in other muscles, whose movements are in reality reflex in their nature. In all these cases the probabilities are that there is a condition of acute hyperæmia or of excessive functional irritability of the spinal cord.

In regard to certain so-called functional palsies; in *diphtheritic paralysis* the irritability of the muscles is often diminished and sometimes destroyed; in *lead palsy* it is generally lost, and, curiously enough, according to my own observation the muscles may recover to a marked degree the power of voluntary motion, without a corresponding restoration of their normal electrical relations.

In *hysterical paralysis* any aid to diagnosis is often of very great value; and it has been asserted that in this class of palsies the preservation of electro-contractility with loss of electro-sensibility is always present, and is of diagnostic import. My experience, however, is very positive that in hysterical palsy both electro-contractility and electro-sensibility are frequently normal. When, however, the paralyzed muscle responds to galvanic currents, and the patient is to a great extent, or altogether, insensible to their passage, a very positive diagnosis of hysteria may be given. The electro-contractility is never seriously compromised in hysterical palsy.

In using galvanism as an aid in *prognosis*, the condition of the muscular contractility is always to be considered in conjunction with the nature of the lesion and the length of time it has existed.

Taking first ordinary *hemiplegia* as the type of *cerebral* palsies, it must be borne in mind that the actual existent amount of paralysis is really the product of two essentially different factors. The nerve-centre is primarily damaged, and after a time the muscle also suffers loss of structural integrity from want of use. The restoration of the nerve-centre does not necessarily involve the restoration of the muscle, so that in a case of hemiplegia of some standing the cerebrum may have recovered itself partially or entirely, and yet the muscle be in such a state of degeneration as to be unable to respond to the impulse transmitted to it from the nerve-centre.

Under these circumstances, galvanic treatment, although unable to affect to any extent the nerve-centres, does great good by restoring the muscular tone. It is manifestly impossible in such a case to determine before treatment how far the nerve-centre has recovered itself, or, in other words, to what extent the existing paralysis is of centric and to what extent it is of muscular origin. When, in a case of apoplectic hemiplegia, there is no recovery at all of the power of voluntary movement after the lapse of six weeks, the prospect of decided improvement from electrical treatment is very gloomy, because the probabilities are altogether in favor of the existence of a serious, persistent centric lesion. If, however, there is some motion, the probabilities of improvement are inversely proportionate to the structural health of the muscles. If the tone and the electro-contractility of these are normal, the centric factor is the chief one in the production of the paralysis, and little good is to be achieved by the use of the galvanic current. On the other hand, if the muscles have undergone a very decided degeneration, much good is to be expected. No hopes of absolute cure should, however, be held out, because, in the great majority of cases, after the muscles have been fully restored the nerve-centre is found to be more or less damaged. The improvement under the use of electricity is usually at first rapid, but after a time ceases altogether, because, the muscles having recovered their tone, it is not possible to affect, to any great extent, the sole remaining cause of the paralysis,—*i.e.*, the centric lesion. Under these circumstances it is useless to continue treatment.

In *infantile paralysis*, early in the attack the galvanic current is of little value in determining the prognosis, excepting that the general law is, that the more rapidly electro-contractility is lost, the more serious is the case. In advanced cases, the duration of the attack and the condition of the electro-contractility in the muscles are both to be considered. If no response at all to an electric current can be obtained, the prognosis is always very grave; although even under such circumstances a decided improvement has occurred in a small percentage of the cases I have treated. If the case be an old one, the preservation of some degree of electro-contractility indicates that the structural lesion in the cord is not a fatal one; and as, under these circumstances, the muscles can always be more or less perfectly restored, the prospect of improvement is very good. The preservation of electro-contractility late in the disorder, when the centric lesion is no longer progressing, is of much more import than it is in the first few weeks or months of the case, when the central trouble may be increasing.

In *peripheral palsies* the prognosis depends rather upon the nature of the nerve-lesion than upon the condition of the muscle; but it must be remembered that when a muscle has absolutely lost its power of responding to any electrical current its restoration is always a matter of difficulty and of some doubt.

In regard to *therapeusis*, the first point to be determined in acute cases is, very often, when to commence electrical treatment. When the lesion is of such nature as not to provoke any irritation of the nerve-centre, no time should be lost. Thus, if a man is unable to use his arm because he has slept with it under his head and thereby paralyzed the nerve by pressure, galvanism should be at once employed.

When, however, the lesion is of such character as of necessity to irritate the nerve-centres, the case is different. The local stimulation of the peripheral nerve-fibres by the electrical current does, in some way not yet definitely understood, affect the nutrition of the nerve-centres; and when these nerve-centres are in a state of active excitement or inflammation, a peripheral galvanic irritation may do serious injury. Hence the rule that when an acute palsy is connected with active irritation of the nerve-centres, galvanism should not be used upon the muscles until the centric disturbance has subsided. Thus, in *hemiplegia* from cerebral hemorrhage the muscles must be allowed to rest not only until all symptoms of centric irritation have passed away, but also until the brain has become so accustomed to the clot that the latter no longer acts as a foreign body. It is usually from three to six weeks before electricity can be used with advantage in these cases. Again, in acute *cerebritis*, *cerebral* or *spinal meningitis*, and *myelitis*, the employment of galvanic currents should be strictly forbidden until a stage is reached when the effects of the inflammation, and not the inflammation itself, are to be dealt with.

When it has been decided to commence the use of galvanism, it is next to be determined what current shall be employed. It has already been shown that there are no inherent mysterious differences in the various currents; yet there is a practical difference, and the clinical rule of choice is, *Always select that current which produces the greatest number of muscular contractions with the least amount of pain;* trying the rapidly-interrupted faradic or the rapidly-interrupted chemical current, and the slowly-interrupted faradic or the slowly-interrupted chemical current, and always, when these fail to elicit response, the slowly-reversed chemical current, which, if necessary, may be increased in strength until the patient can no longer bear the pain.

The current having been selected, the *individual muscles* must be galvanized at each séance.

After what has been said previously, it is not necessary to speak at this point as to the best methods of applying the currents to the muscles, but only to insist upon the fact that it is not so much the electricity as the contractions induced by it which benefit the palsied parts, and that consequently the electro-motor points of the muscles should always be separately reached. The diagrams given in the Appendix will point out more clearly than would pages of description the approximate positions of the motor points, which vary somewhat in their location in various individuals. Some deep-seated muscles we are not able to reach directly, but we can reach them indirectly by galvanizing the nerves which supply them.

There are certain precautionary rules which must never be lost sight of in the galvanic treatment of palsies. Pain is an evil, and its infliction is always to be avoided as far as possible. Hence the rule never to use stronger currents than is necessary. It is very possible to fatigue a healthy muscle, much more a diseased one. A weak muscle may be greatly injured by being over-fatigued. Hence the rule that currents are not to be applied to muscles sufficiently long at a time to induce fatigue. In general, an electrical séance should last from ten to twenty minutes, no one muscle being subjected to the currents for more than five minutes, and it may be repeated daily, or three times a week.

Sensory System.—Affections of the sensory nerves are of three kinds,—pain, hyperæsthesia, and anæsthesia. There are, of course, distinct states or disorders, which may exist separately or conjointly: as an instance of the co-existence of pain and anæsthesia may be mentioned the anæsthesia dolorosa of Romberg. The use of electricity for the relief of these disorders is almost entirely empirical,—indeed, is often purely experimental in an individual case, as no clinical laws regulating the use or enabling us to decide as to the applicability of the agency have as yet been worked out.

It may be laid down, however, as an axiom, that the galvanic current is powerless to relieve the *pain* of phlegmonous *inflammations*, and that its use should be restricted chiefly to nervous pain or neuralgia. It is also true that the currents are possessed of no therapeutic power over neuralgia dependent upon central organic lesions; this is also probably true of such neuralgias as *migraine*, *malarial hemicrania*, and *toxic neuralgias*, in which, although there is no perceptible organic lesion, there is some deep-seated, inherent deficiency either in the central nervous system or in the constitution or condition of the patient.

In *rheumatic neuralgias*, such as *sciatica*, electricity sometimes does great good, but perhaps more often fails. I have seen it effect the greatest good, and I have seen it aggravate the disorder. My experience has not been sufficient to allow me to speak authoritatively, but it appears to indicate that the currents are most successful when the stage of acute inflammation is past and when the pain is maintained by some persistent condition or habit of the nerve-trunk. In regard to the selection of the current, my experience is that it must be purely empirical. The most usually successful is a very mild (four to eight cells) chemical current, which should be passed steadily for ten minutes down the nerves. It should not be so strong as to give actual pain, and must not be interrupted. As in the great majority of cases this method of application yields the best results, it should always be tried first. When it does good, it *nearly always* affords relief after, at the most, two or three sittings. Some cases receive most benefit from a rapidly-interrupted faradic current, which should therefore be tried if the continuous current fail. To the employment of electricity should of course always be added the proper constitutional treatment of the case.

In *hysteria*, in some cases whose nature is very obscure, and rarely as a sequela or result of a serious cerebral or spinal lesion, which may have been more or less completely recovered from, there exist *local anæsthesias* of the skin. When these are not dependent upon a too serious organic lesion, they are often very much benefited, or even cured, by the use of the electric brush. This should be large and composed of fine wires, whilst the other electrode should consist of a large, well-wetted sponge, placed upon a distant part of the body. Either the faradic or the chemical current may be employed; in either case it should be a very strong one.

APPLICATION TO THE NERVE-CENTRES, AND USE AS A TONIC.—Galvanism in various forms has been applied locally to the nerve-centres in various diseases. In regard to the brain, I have never yet met with any clear clinical evidence of good having been accomplished; and, with our present physiological knowledge, it is difficult to imagine in what way or under what circumstances cerebral galvanization can produce good results On the other hand, harm certainly has been wrought by the application of strong currents to the head. Galvanic currents passed through the brain can act only as irritants, and I agree entirely with the dictum of Cyon (*Principes d'Electrothérapie*, Paris, 1873), that galvanization of the head ought to be abandoned.

An enormous amount of influence in all sorts of diseases has been claimed for the so-called *galvanization of the sympathetic*. In this application an olive-shaped electrode is pressed firmly into the auriculo-maxillary fossa, whilst a large sponge electrode is placed over or by the side of the sixth and seventh cervical vertebræ. For anatomical reasons, I do not believe it possible in this method to affect the upper cervical sympathetic ganglion; and the physiological and clinical evidence seems to me to point to the same conclusion. The ganglion is placed deeply beneath the carotid artery, and so situated that any current traversing it *en route* to the other pole, as usually applied, would have to pass through the vertebræ. The laws of electrical conduction, however, show that the currents would seek the routes of least resistance, so that it is *a priori* improbable that any appreciable portion of the galvanism would pass through the ganglion.

Leaving all this aside, the physiological proof that the currents of appreciable power do not reach the ganglion are, to my mind, very absolute. When the slightest galvanic stimulus is applied to the bared ganglion, the results which follow are uniform, constant, and so apparent that a child can see them: they are dilatation of the pupil, and contraction of the vessels of the eye, ear, etc., and *nothing more*. These results do *not* follow the application of the currents in man, as above described. It has been asserted that the vessels of the retina have been seen to contract; but Prof. William F.

Norris, one of the best ophthalmologists in the country, has very closely observed the retinal vessels under these circumstances, and has never been able to detect the slightest change. Moreover, some of the observers who have seen the vessels alter state that they dilate, while others affirm that they contract, or that they sometimes contract and sometimes dilate. If the vessels change under the influence of the current, why does not the pupil? Any unprejudiced observer can be convinced at once that it does not alter, and any prejudiced and not very skilful ophthalmologist may find in the retinal vessels what he expects. Drs. Beard and Rockwell strongly insist upon the possibility of galvanizing the cervical sympathetic, yet they acknowledge (*loc. cit.*, p. 129) "that the ordinary therapeutical measures for electrizing the sympathetics *do not* produce the same effects as electrizing the ganglia." This being so, it would seem unnecessary to discuss the subject further: yet I shall analyze somewhat the evidence upon which the gentlemen mentioned, along with other electro-therapeutists, rest an opinion so seemingly opposed to all scientific induction. This evidence, as founded on the large series of experiments of Drs. Beard and Rockwell, is embraced in the following paragraphs:

First. The alleged action on the retinal vessels.

Second. A hypnotic effect was sometimes perceptible, but *only* in the very nervous and impressionable.

Third. A sensible perspiration was caused when very strong currents were used.

Fourth. The pulse was sometimes accelerated, sometimes slackened.

In regard to the evidence contained in the first paragraph; as already stated, the results of observations are altogether contradictory, even Beard and Rockwell stating that "much seemed to depend on the temperament and condition of the individual; what would cause contraction in one would cause dilatation in another." The changes in the retinal vessels could not, under these circumstances, have been due to an action of the galvanism upon a ganglion, stimulation of which *always* produces contraction of the vessels: evidently, if alterations of the vessels really occurred, they were the results of psychical or other influences, and not directly due to the galvanic current.

As none of the phenomena mentioned in the second, third, and fourth propositions are produced when the bared ganglia is galvanized, and as all of them are producible by pain or nervous excitement, it seems very plain that, like the asserted retinal changes, they must have had their origin in the psychical disturbance of observer or patient.

Very great therapeutic value has been attached by various writers to the effect of *galvanization of the spinal cord.* As in the case of the sympathetic, most opposite opinions are held by equally high authorities: one asserting that a downward spinal current dilates and an upward one contracts the vessels of the cord, whilst another most strenuously insists that upward currents contract the vessels and downward currents dilate them. The same line of reasoning that has here been given in regard to the sympathetic nerve applies to the spinal cord. The infinitely weak current formed between a silver grooved director and a pair of iron forceps, moistened with the fluid of the body, will induce when applied to the bared cord very distinct evidences of functional excitement, in the form of spasms; and yet no current I have ever been able to apply to the spine in patients has ever caused a tremor in the muscles other than those of the back. If spinal currents do good directly, I conceive it must be by an action upon the nerve-peripheries; for it is entirely possible that such an action may affect the nutrition of the cord. Moreover, in some of the diseases in which the measure has been practiced with most success, the very great power of the emotions is notorious; and I conceive electricity often cures by acting on the mental or moral nature. Of course the cure may be no less real and important on this account. In that peculiar affection allied to hysteria, variously known as *spinal irritation*, *spinal anæmia*, etc., I have seen the application of electricity to the back of the greatest service. Sometimes a rapidly-interrupted, strong faradic current has appeared to be most effectual; sometimes a moderate, continuous chemical current has best suited the case. In *spinal congestion*, and in *chronic spinal inflammations* of all forms, I have used downward chemical currents in a large number of cases, but in every instance other measures were at the same time employed, and only in a very few cases has there been any definite evidence of the galvanism being of any service. From ten to twenty-five cells may be employed, the positive pole being applied for fifteen to twenty minutes upon the nape of the neck, the negative over the coccyx or on the centre of the lumbar vertebræ.

It has recently been shown that galvanism has some tonic powers, and may be used as such in cases of simple debility or nervous exhaustion without any definite lesions. From what we know of its physiological action, it is reasonable to suppose that the force must be able to modify the circulation of every part that has muscular fibres in itself or in its blood-vessels; and such parts constitute the great bulk of the body. It has also been shown by Dr. S. Weir Mitchell that it is capable of temporarily elevating the general bodily temperature. Whether its action is solely by modifying the circulation and causing muscular contractions, or whether it has also a more direct influence upon the nutritive cell actions, is uncertain. Beard and Rockwell* employ two methods of application, which they denominate general faradization and central galvanization, as follows:

General Faradization.—In practicing this, the patient should put the feet upon a copper plate, which serves as one electrode, or should have a large, moistened sponge placed over the coccyx, whilst a large sponge electrode is passed over the surface of the body. The movable electrode should be first placed upon the forehead, then back of the ears, a mild current being used. It may then be pressed firmly over the sixth and seventh cervical vertebræ, and a powerful current employed; then it should be passed to the posterior cervical triangle just by the posterior border of the sterno-cleido-mastoid muscle; then to the middle of the spine, where very strong currents are usually well borne; then down the chest to the pit of the stomach, and finally to the extremities. Beard and Rockwell give the following as the usual length and proportion of the séance: head, one minute; neck and cervical spine, four minutes; back, three minutes; abdomen, three minutes; upper and lower extremities, four minutes.

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* A Practical Treatise on the Medical and Surgical Uses of Electricity. New York: Wm. Wood & Co. 1875.

In employing this method, at first the currents should not be too powerful, afterwards they should be made as strong as can be borne without pain. The séances should be held two or three times a week.

Central Galvanization.—"The object in central galvanization is to bring the whole central nervous system—the brain, sympathetic and spinal cord, as well as the pneumogastric and depressor nerves—under the influence of the galvanic current. One pole (usually the negative) is placed at the epigastrium, while the other is passed over the forehead and top of the head, by the inner borders of the sterno-cleido-mastoid muscles, from the mastoid fossa to the sternum, at the nape of the neck, and down the entire length of the spine." In applying the pole to the head, the hair should be wetted, or, if this be objected to, the application should be made to the top of the head, locally dampened, and over the prominences back of the ears. Care should be taken not to interrupt the current, and in increasing it to use the rheostat no oftener than is absolutely necessary. The séance should be repeated twice or three times a week, and should be arranged as follows: head, one to two minutes (six to eight cells); neck, both sides, one to five minutes (ten to fifteen cells); back, three to six minutes (ten to thirty cells).

In regard to the choice of these plans, Beard and Rockwell affirm that general faradization is to be preferred where great *muscular* debility exists; central galvanization where there is rather a *nervous* exhaustion, as in *hysteria* and *chorea*, *hypochondriasis*, etc. In many cases the best effects are to be obtained by alternating the modes of application, either from day to day or from week to week.

My own experience leads me to prefer decidedly the induced current as a tonic. The plan which I have adopted is to affix a large stationary electrode to the feet, or during part of the séance to the coccygeal region, and then to apply slowly and successively a smaller electrode to the motor points of the various muscles of the upper extremities, neck, trunk, and lower extremities; also to place for longer periods one electrode over the larger abdominal viscera. The most marked results have been met with in large, relaxed multipara, with a tendency to uterine displacement. In these cases one pole has been introduced high up into the vagina, and care taken especially to act upon the broad ligaments.

APPENDIX.

ON THE ART OF PRESCRIBING MEDICINES.

In the practical use of remedies, very much depends upon the methods of their combination, and, so far as concerns the reputation of the physician, no little importance is to be attached to the mere prescription-writing. The recipes of the master are very widely seen, and he who is incorrect in the grammar or spelling of his English or Latin, or departs without reason from the traditional forms, lays himself open to ridicule, than which nothing is more damaging. A crooked, bad chirography is the traditional mark of learning; but absolute plainness should be a *sine quâ non* in the writer of prescriptions. This should also apply to abbreviations: these should be of such a character as not only to be readily made out, but also to be so evident as to afford no shelter to the apothecary whose carelessness has led to serious error. In the case of alkaloids and other powerful remedies, the chief name at least should be written in full. In writing the prescription, all the ingredients should first be put down, then the number of doses should be decided upon, and the individual amounts of each substance marked seriatim. It is a very good custom always to place first upon the list the strongest of the drugs employed. Without further comment, the following recipes are appended, simply as examples of the method of writing prescriptions: the first two only are given in full, with date, signature, etc.:

John Smith, Esq.
℞ Tr. cantharidis, fʒss;
Tr. ferri chlor., f℥ss.
M.
S.—Fifteen drops three times a day.
July 1, 1875. S. W. W.

℞ Ol. morrhuæ, f℥ii;
Ol. amygdalæ amaræ, gtt. vi;
Mucil. acaciæ, f℥iv.
M. et ft. emuls.
S.—Tablespoonful three times a day.

℞ Cerat. cantharidis, q. s.
Ft. emplastrum iii × iv unc.
S.—Use as directed.

Jno. Jones, Esq.
℞ Syr. scillæ,
Syr. senegæ, āā f℥i;
Liq. morphiæ sulph., f℥ss;
Syr. tolutan., q. s. ad f℥iii.
M.
S.—Dessertspoonful four times a day.
July 1, 1875. R. S. T.

℞ Extr. chirettæ, gr. xx;
Strychniæ, gr. i;
Ferri pulv., ʒi;
Oleores. piperis, gr. viii.
M. et ft. mas. in pil. xx div.
S.—One before meals.

℞ Quiniæ sulph., gr. xxxvi;
Tr. ferri chloridi, fʒiii;
Glycerinæ,
Syrupi, āā f℥iss.
M.
S.—Dessertspoonful after meals.

℞ Hydrarg. chl. mitis, gr. vi;
Sacchari, q. s.
M. et ft. pulv. vi.
S.—Use as directed.

℞ Acidi tannici, ʒi.
Ft. pulv. in chart. vi div.
S.—Use as directed.

℞ Extr. colocynth. comp., gr. xii;
Extr. belladonnæ, gr. ii;
Alöes, gr. xviii;
Ol. caryophyl., gtt. xii.
M. et ft. pil. xii.
S.—One at bedtime.

℞ Sennæ, ʒiii;
Magnesii sulphatis,
Mannæ, āā ℥ss;
Fœniculi, ʒi;
Aquæ bullientis, Oss.
Macera per horam in vase leviter clauso et cola.
S.—*Black Draught.* Dose.—A teacupful every six hours, until it operates.*

The art of combining remedies is not a difficult one; but in practice certain principles should not be lost sight of. Chief of these are, to prescribe as few remedies as possible, and to use no powerful drug without a very distinct idea of what it is intended to do. Whenever it is desired to give a powerful remedy in increasing doses until its physiological effect is produced, it should always be given by itself. Thus, it may be necessary to give arsenic so as to impress the system, at the same time that iron is indicated; but the two remedies should be given separately, so that the dose of either can be increased or diminished independently of the other.

The principles of combination, formulated below, were long ago enunciated by Dr. Paris, but are to-day as imperative as ever. Medicines are combined:

First. To augment, correct, or modify the action of a medicine. Thus, purgatives act much more kindly when a number of them are united together. The chief reason of this probably is, that as different remedies affect different portions of the gut, the whole intestine is best reached by a union of the diverse substances. It may take an intense irritation of the mucous membrane to purge as actively as does a mild irritation of both the mucous membrane and the muscular coat. In the case of neurotics, the principle has a very limited action, because so many of this class of remedies are physiologically more or less antagonistic; yet sometimes the principle can be advantageously applied: thus, the anæsthesia of chloroform or ether may be prolonged by a hypodermic injection of morphia; and chloral and morphia certainly make a mixture which is much more powerfully hypnotic than is either of the substances separately.

Second. To obtain the joint action of two or more diverse remedies. Thus, in a cough mixture, morphia may be included to quiet the cough, whilst ipecacuanha and squill (in accordance with the first principle) are added to affect the mucous membrane. The application of this principle requires caution, or the practitioner will be led into that chief abomination, polypharmacy. It is worse than futile to attempt to prescribe for every symptom. It is the underlying cause of the disorder or the under-stratum of bodily condition which must be sought out and prescribed for simply.

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* These prescriptions are printed as usually written, with abbreviations. The full sentences of directions to the apothecary are:—Misce et fiat emulsio—Fiat emplastrum iii × xiv unciarum—Misce—Misce et fiat massa in pilulas viginti dividendus—Misce et fiat pulveres sex—Fiat pulvis in chartulas duodecim dividendus—Misce et fiat pilulæ duodecim.

Third. To obtain a special combination, which is really a new remedy, or which experience has shown acts almost as a new remedy. Thus, when to iodide of potassium in solution corrosive sublimate is added, a new chemical compound is formed, which experience has shown to be of great value in syphilitic diseases. Griffith's antihectic mixture is another instance of the use of chemical changes, the proto-carbonate of iron being formed out of the sulphate of the metal and the carbonate of potassium. In the famous Dover's powder no chemical change occurs, but the ordinary action of opium upon the skin is so enhanced that the combination may be looked upon almost as a new remedy.

Fourth. To afford a suitable form. Thus, acacia is added to make an emulsion, or confection of rose to make a pill. In the choice of excipients, care should be exercised to select a substance free from medical properties, having no chemical incompatibility with the medicinal agent, and of suitable physical character. Bread-crumbs often make a good basis for pills; but with nitrate of silver they are chemically incompatible, on account of the chlorides in them. When writing a prescription, the utmost care should be taken to use such excipients that the combination should not only be attractive to the eye, but also as little repulsive to the palate as may be. Whenever possible, the pill form should be employed with bitter or disagreeable medicines. The pill may be readily coated with silver-foil; tonic pills may be coated with iron by shaking or rolling them in ferri pulvis whilst soft and sticky. Sugar-coated pills and "compressed pills" are apt to get so hard and insoluble that their use requires caution. In regard to mixtures, flavoring oils should be freely used, and the power of glycerine to conceal the disagreeable taste of many substances should be remembered.

Incompatibilities.—In combining remedies, the subject of incompatibilities must never be lost sight of. The kinds of incompatibility are two in number,—physiological and chemical. The first of these it would require large space to discuss fully, and any one familiar with the text of the book, if possessed of the slightest reasoning powers, can readily make all necessary deductions.

In many works on materia medica long lists of chemical incompatibilities are given in the accounts of individual drugs. These lists have seemed to me useless, as I have never met with a student who could commit and retain them. Moreover, they contain so much matter of no practical use that the valuable portion is hidden out of sight. A certain amount of chemical knowledge is essential to the student, and is not to be taught in a book like the present. He who would ignorantly combine sulphuric acid and a carbonate needs to re-study his chemical text-book. All that I shall do here is to point out certain principles and a few especial reactions. The following rules may serve for a guide:

Soluble salts which can, by mutual decomposition, form an insoluble compound, will undergo such decomposition when they meet in solution, and will precipitate, unless in some very rare instances, in which a double salt is formed.

Soluble salts which are not capable of forming an insoluble salt never precipitate, and rarely undergo decomposition when they meet in solution.

Mineral acids decompose salts of the weaker (carbonic, acetic, etc.) acids, and form ethers with alcohol and alcoholic preparations.

Alkalies precipitate the alkaloids and the soluble non-alkaline metallic salts.

Glucosides, such as santonin and colocynthin, should not be prescribed with free acids or emulsin.

Tannic acid and all substances containing it are incompatible with alkaloids and drugs containing them, with albumen and gelatine, and with most soluble metallic salts used in medicine.

Iodine and soluble *iodides* are incompatible with the alkaloids and the substances containing them, as well as with most soluble metallic salts. The *iodide of potassium** should always be prescribed alone, or only in combination with corrosive sublimate (with which it forms a double salt), or with iodine itself.

Tinctures and other *alcoholic preparations* containing resin precipitate the latter when water is added.

Nitrate of silver should always be prescribed alone, or in combination with opium only. Most vegetable extracts decompose it, and with creasote it is said to make an explosive compound.

Corrosive sublimate is incompatible with almost everything, and should be given in simple syrup; even the compound syrup of sarsaparilla is said to decompose it.

Syrup of squill containing acetic acid is incompatible with carbonate of ammonium, but not with the chloride.

Acetate and subacetate of lead are incompatible with almost everything, but are nevertheless frequently used in lotion with opium, the insoluble compound formed being therapeutically active.

Vegetable infusions are generally incompatible with metallic salts.

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* Death has resulted from a prescription containing strychnia and iodide of potassium, all the alkaloid being taken at the last dose.

WEIGHTS AND MEASURES OF THE UNITED STATES PHARMACOPŒIA.

Pound,	℔	=	**12 Ounces.**	**Gallon,**	**C**	=	**8 Pints.**
Ounce,	℥	=	**8 Drachms.**	**Pint,**	**O**	=	**16 Fluidounces.**
Drachm,	ʒ	=	**3 Scruples.**	**Fluidounce,**	**f℥**	=	**8 Fluidrachms.**
Scruple,	℈	=	**20 Grains.**	**Fluidrachm,**	**fʒ**	=	**60 Minims**
Grain,	**gr.**	=	**1 Grain.**	**Minim,**	♏	=	**1 Minim.**

WEIGHTS AND MEASURES OF THE METRICAL OR FRENCH SYSTEM.

MEASURES OF LENGTH.

One Myriametre = 10,000 Metres.
One Kilometre = 1,000 Metres.
One Hectometre = 100 Metres.
One Decametre = 10 Metres.
One METRE = the ten-millionth part of a quarter of the meridian of the earth.
One Decimetre = the tenth part of one Metre, or 0.1 Metre.
One Centimetre = the hundredth part of one Metre, or 0.01 Metre.
One Millimetre = the thousandth part of one Metre, or 0.001 Metre.

WEIGHTS.

One Myriagramme = 10,000 Grammes.
One Kilogramme = 1,000 Grammes.
One Hectogramme = 100 Grammes.
One Decagramme = 10 Grammes.
One GRAMME = the weight of a cubic Centimetre of water at 4° C.
One Decigramme = the tenth part of one Gramme, or 0.1 Gramme.
One Centigramme = the hundredth part of one Gramme, or 0.01 Gramme.
One Milligramme = the thousandth part of one Gramme, or 0.001 Gramme.

MEASURES OF CAPACITY.

One Myrialitre = 10 cubic Metres, or the measure of 10 Milliers of Water.
One Kilolitre = 1 cubic Metre, or the measure of 1 Millier of Water.
One Hectolitre = 100 cubic Decimetres, or the measure of 1 Quintal of Water.
One Decalitre = 10 cubic Decimetres, or the measure of 1 Myriagramme of Water.
One LITRE = 1 cubic Decimetre, or the measure of 1 Kilogramme of Water.
One Decilitre = 100 cubic Centimetres, or the measure of 1 Hectogramme of Water.
One Centilitre = 10 cubic Centimetres, or the measure of 1 Decagramme of Water.
One Millitre = 1 cubic Centimetre, or the measure of 1 Gramme of Water.

RELATION OF WEIGHTS AND MEASURES OF THE U. S. PHARMACOPŒIA TO EACH OTHER.

In distilled water at the temperature of 60°.

One Pound	=	0.7900031 Pint	=	6067.2238 Minims.
One Ounce	=	1.0533376 Fluidounces	=	505.6019 Minims.
One Drachm	=	1.0533376 Fluidrachms	=	63.2002 Minims.
One Scruple	=	. . . .	=	21.0667 Minims.
One Grain	=	. . . .	=	1.0533 Minims.
One Gallon	=	10.1265427 Pounds	=	58328.8862 Grains.
One Pint	=	1.2658178 Pounds	=	7291.1107 Grains.
One Fluidounce	=	0.9493633 Ounce	=	455.6944 Grains.
One Fluidrachm	=	0.9493633 Drachm	=	56.9618 Grains.
One Minim		. . . .	=	0.9493 Grain.

RELATION OF MEASURES OF THE U. S. PHARMACOPŒIA TO CUBIC MEASURE.

One Gallon	=	231. Cubic Inches.	One Fluidrachm	=	0.22558 Cubic Inch.
One Pint	=	28.875 Cubic Inches.	One Minim	=	0.00375 Cubic Inch.
One Fluidounce	=	1.80468 Cubic Inches.			

RELATION OF WEIGHTS OF THE U. S. PHARMACOPŒIA TO METRICAL WEIGHTS.

Fractions of a grain in Milligrammes.

Grain.		Milligrammes.
$\frac{1}{64}$	=	1.012
$\frac{1}{60}$	=	1.079
$\frac{1}{50}$	=	1.295
$\frac{1}{48}$	=	1.349
$\frac{1}{40}$	=	1.619
$\frac{1}{36}$	=	1.799
$\frac{1}{30}$	=	2.159
$\frac{1}{25}$	=	2.591
$\frac{1}{24}$	=	2.699
$\frac{1}{20}$	=	3.239
$\frac{1}{16}$	=	4.049
$\frac{1}{15}$	=	4.319
$\frac{1}{12}$	=	5.399
$\frac{1}{10}$	=	6.479
$\frac{1}{8}$	=	8.098
$\frac{1}{6}$	=	10.798
$\frac{1}{5}$	=	12.958
$\frac{1}{4}$	=	16.197
$\frac{1}{3}$	=	21.597
$\frac{1}{2}$	=	32.395

Grains in equivalent metrical weights.

Grains.		Centigrammes.
1	=	6.479
		Decigrammes.
2	=	1.295
3	=	1.943
4	=	2.591
5	=	3.239
6	=	3.887
7	=	4.535
8	=	5.183
9	=	5.831
10	=	6.479
12	=	7.775
15	=	9.718
		Grammes.
16	=	1.036
20	=	1.295
24	=	1.555
25	=	1.619
30	=	1.943
40	=	2.591
50	=	3.239
60	=	3.887

Drachms, Ounces, and Pounds in equivalent metrical weights.

Drachms.		Grammes.
1	=	3.887
2	=	7.775
		Decagrammes.
3	=	1.166
4	=	1.555
5	=	1.943
6	=	2.332
7	=	2.721
Ounces.		
1	=	3.1103
2	=	6.2206
3	=	9.3309
		Hectogrammes.
4	=	1.2441
5	=	1.5551
6	=	1.8661
7	=	2.1772
8	=	2.4882
9	=	2.7992
10	=	3.1103
11	=	3.4213
Pounds.		
1	=	3.7324
2	=	7.4648
		Kilogrammes.
3	=	1.1197

RELATION OF METRICAL WEIGHTS TO WEIGHTS OF THE U. S. PHARMACOPŒIA.

Metrical Weights.		*Exact equivalents in grains.*	*Approximate equivalents in grains.*
Milligrammes.			
1	=	.0154	1/65
2	=	.0308	1/32
3	=	.0463	1/22
4	=	.0617	1/16
5	=	.0771	1/13
6	=	.0926	1/11
7	=	.1080	1/9
8	=	.1234	1/8
9	=	.1389	1/7
Centigrammes.			
1	=	.1543	1/6
2	=	.3086	1/3
3	=	.4630	6/13
4	=	.6173	7/11
5	=	.7717	3/4
6	=	.9260	9/10
7	=	1.0803	1
8	=	1.2347	1 1/4
9	=	1.3890	1 1/3
Decigrammes.			
1	=	1.543	1 1/2
2	=	3.086	3
3	=	4.630	4 2/3
4	=	6.173	6
5	=	7.717	7 1/2
6	=	9.260	9
7	=	10.803	11
8	=	12.347	12 1/3
9	=	13.890	14

Metrical Weights.		*Exact equivalents in grains.*	*Approximate equivalents in Troy Weight.*
Grammes.			
1	=	15.434	gr. xv.
2	=	30.868	ʒss.
3	=	46.302	℈ij.
4	=	61.736	ʒi.
5	=	77.170	℈iv.
6	=	92.604	ʒiss.
7	=	108.038	℈vss.
8	=	123.472	ʒij.
9	=	138.906	℈vij.
Decagrammes.			
1	=	154.340	ʒiiss.
2	=	308.680	ʒv.
3	=	463.020	ʒviiss.
4	=	617.360	ʒx.
5	=	771.701	ʒxiij.
6	=	926.041	ʒxv.
7	=	1,080.381	ʒxviij.
8	=	1,234.721	ʒxx.
9	=	1,389.062	ʒxxiij.
Hectogrammes.			
1	=	1,543.402	℥iii ℈v.
2	=	3,086.804	℥vj ʒiij.
3	=	4,630.206	℥ix ʒv.
4	=	6,173.609	℔i ʒvij.
5	=	7,717.011	℔i ℥iv.
6	=	9,260.413	℔i ℥vij.
7	=	10,803.816	℔i ℥x ʒiv.
8	=	12,347.218	℔ij ℥i ʒv.
9	=	13,890.620	℔ij ℥v.
Kilogramme.			
1	=	15,434.023	℔ij ℥viij.
Myriagramme.			
1	=	154,340.023	℔ xxvi ℥ix ʒiv.

TABLE OF THE PROPORTION BY MEASURE OF ALCOHOL (SP. GR. 0.825) CONTAINED IN ONE HUNDRED PARTS OF DIFFERENT WINES, ETC.*

Lisa (mean)	25.41
Raisin wine (mean)	25.12
Marsala [Sicily madeira] (mean)	25.09
strongest (J.)	21.10
weakest (J.)	19.90
Port, strongest	25.83
mean	22.96
weakest	19.00
strongest (C.)	20.49
mean (C.)	18.68
weakest (C.)	16.80
strongest (J.)	23.20
weakest (J.)	20.70
White port (C.)	17.22
Madeira, strongest	24.42
mean	22.27
weakest	19.24
strongest (C.)	20.35
strongest (J.)	19.70
weakest (J.)	19.00
Sercial madeira	21.40
Ditto (C.)	18.50
Sherry, strongest	19.81
mean	19.17
weakest	18.25
strongest (C.)	19.31
mean (C.)	18.47
weakest (C.)	16.96
Amontillado (C.)	15.18
strongest (J.)	24.70
weakest (J.)	15.40
Teneriffe	19.79
Teneriffe (C.)	16.61
Colares	19.75
Lachryma Christi	19.70
White Constantia	19.75
Red Constantia	18.92
Lisbon	18.94
Ditto (C.)	19.09
Bucellas	18.49
Red madeira (mean)	20.35
Cape muscat	18.25
Cape madeira (mean)	20.51
Grape wine	18.11
Calcavella (mean)	18.65
Vidonia	19.25
Alba flora	17.26
Zante	17.05
Malaga	17.26
White hermitage	17.43
Roussillon (mean)	18.13
Claret (strongest)	17.11
mean	15.10
weakest	12.91
ditto (F.)	14.73
vin-ordinaire (C.)	10.42
Château-Latour, 1825 (C.)	9.38
first growth, 1811 (C.)	9.32
strongest (J.)	11.10
weakest (J.)	9.10
Malmsey madeira	16.40
Ditto (C.)	15.60
Lunel	15.52
Ditto (F.)	18.10
Shiraz	15.52
Ditto (C.)	15.56
Syracuse	15.28
Sauterne	14.22
Burgundy (mean)	14.57
strongest (J.)	13.20
weakest (J.)	10.10
Hock (mean)	12.08
strongest (J.)	13.00
weakest (J.)	9.50
Nice	14.63
Barsac	13.86
Tent	13.30
Champagne (mean)	12.61
Ditto (F.)	12.20
Ditto, strongest (J.)	14.80
weakest (J.)	14.10
Red hermitage	12.32
Vin de Grave (mean)	13.37
Frontignac (Rives Altes)	12.79
Ditto (C.)	12.29
Côte rôtie	12.32
Tokay	9.88
Rudesheimer, first quality (C.)	10.14
inferior (C.)	8.35
Hambacher, first qual. (C.)	8.88
Catawba (Stearns)	8 to 11

Cider, highest average	9.87
lowest average	5.21
Perry, average of four samples	7.26
Mead	7.32
Ale (Burton)	8.88
Ale (Edinburgh)	6.20
Ale (Dorchester)	5.56
Brown stout	6.80
London porter	4.20
London small beer	1.28
Brandy	53.39
Rum	53.68
Gin	51.60
Scotch whisky	54.32
Irish whisky	53.90

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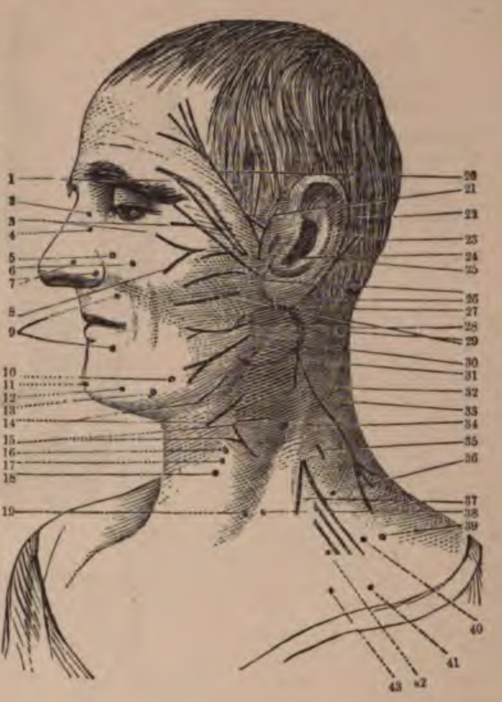
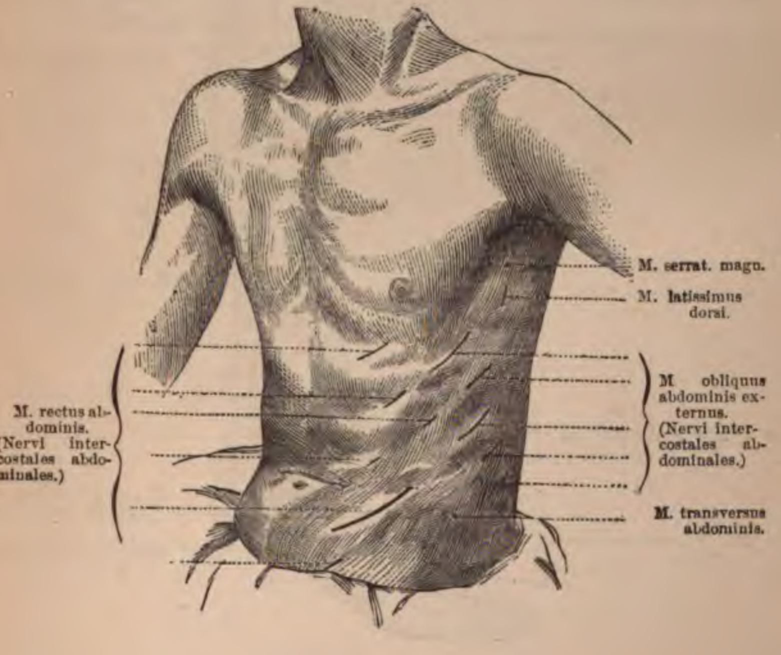
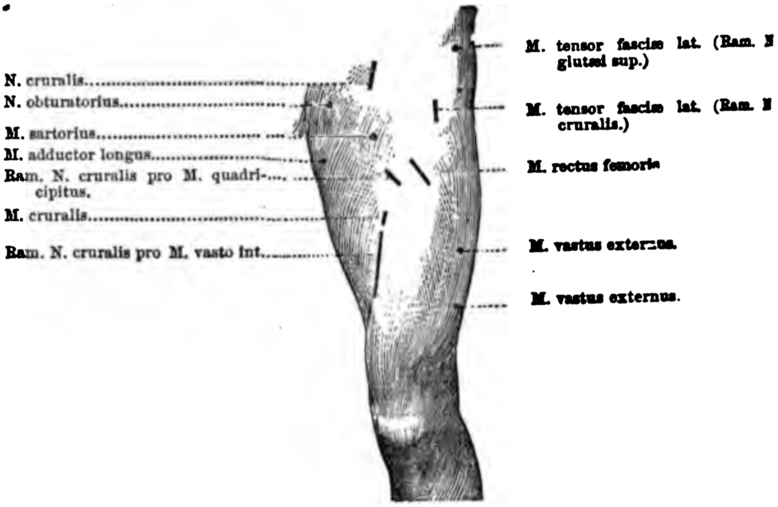
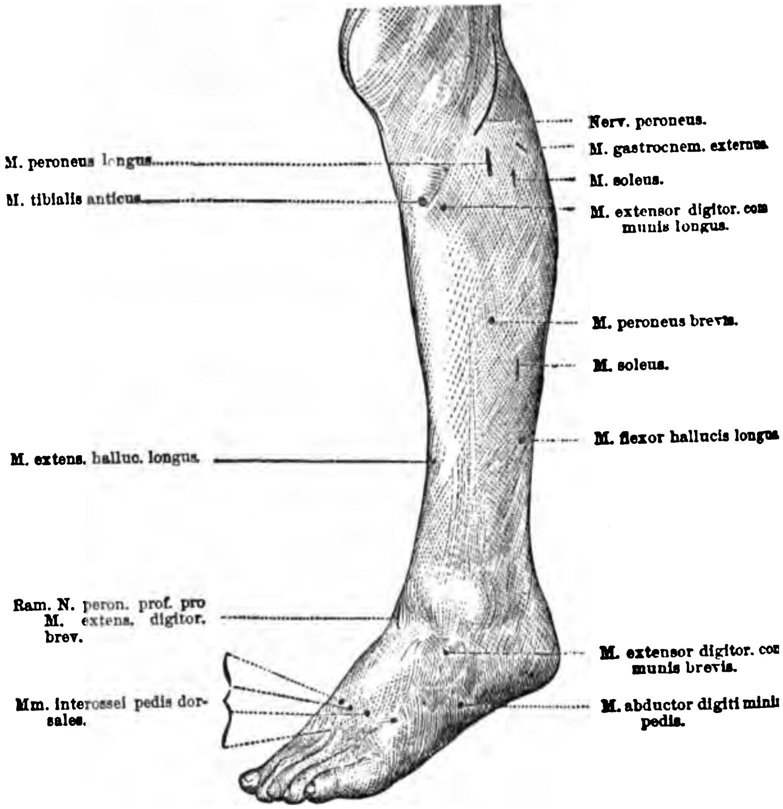
* The analyses whose results are given in this table were mostly made by Mr. Brande. When no mark is attached, the quotation is upon his authority. When the mark (F.) is added, the analysis was made by Julia-Fontenelle; (C.) by Professor Christison; (J.) by Dr. H. Bence Jones.

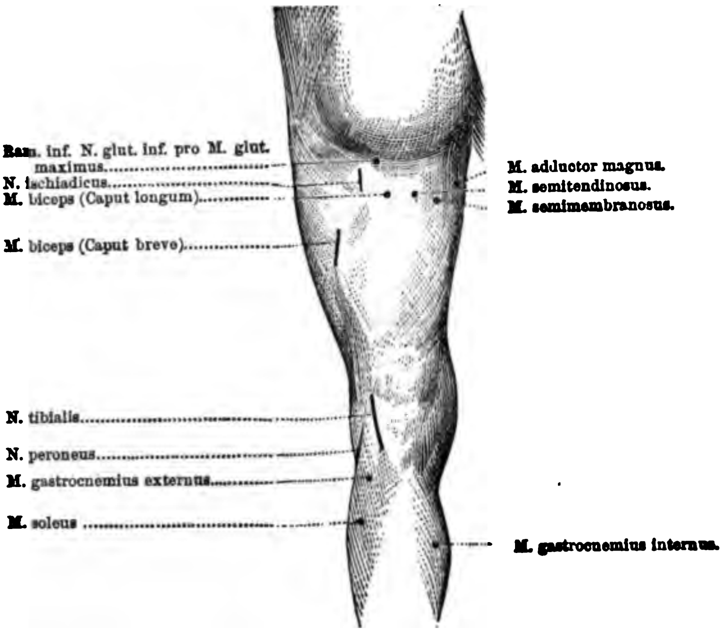


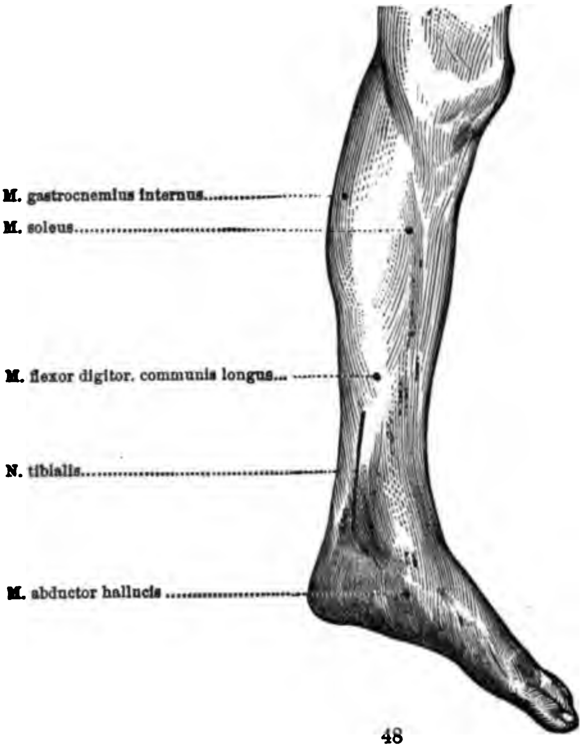
1, M. corrugator supercil.; 2, M. compressor nasi et pyramidal. nasi; 3, M. orbicular. palpebr.; 4, M. levator lab. sup. alæque nasi; 5, M. levator lab. sup. propr.; 6, M. zygomatic. minor; 7, M. dilatat. narium ant. et post.; 8, M. zygomatic. major; 9, M. orbicularis oris; 10, Ram. comm. pro Mm. triangular. et levator menti; 11, M. levator menti; 12, M. quadratus menti; 13, M. triangularis menti; 14, Rami subcutan. colli N. facial.; 15, Rami cervical. pro Platysmat.; 16, M. sterno-hyoideus; 17, M. omo-hyoideus; 18, M. sterno-thyroideus; 19, M. sterno-hyoideus; 20, M. frontalis; 21, Mm. attrahens et attollens auriculæ; 22, Mm. retrahens et attoll. auriculæ; 23, Musc. occipitalis; 24, Nerv. facialis; 25, Ram. auricular. post. prof. N. facialis; 26, M. stylo-hyoideus; 27, M. digastricus; 28, Rami buccales, N. facialis; 29, M. splenius capitis; 30, Rami subcutan. maxill. infer.; 31, Ram. ext. N. accessorii Willisii; 32, M. sterno-cleido-mastoideus; 33, M. cucullaris; 34, M. sterno-cleido-mastoideus; 35, M. levator. anguli scapulæ; 36, N. thoracic. post. (Mm. rhomboidei); 37, N. phrenicus; 38, M. omo-hyoid; 39, N. thoracic. lateral. (M. serrat. magu.); 40, N. axillaris; 41, Ram. plex. brachialis (N. musculocutan., pars N. mediani); 42, N. thoracic. ant. (M. pectorales).

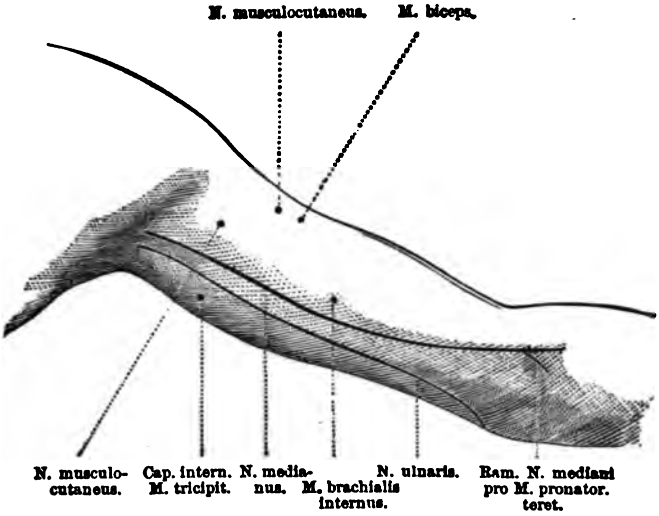

M. serrat. magn.
M. latissimus dorsi.
M. rectus abdominis. (Nervi intercostales abdominales.)
M obliquus abdominis externus. (Nervi intercostales abdominales.)
M. transversus abdominis.

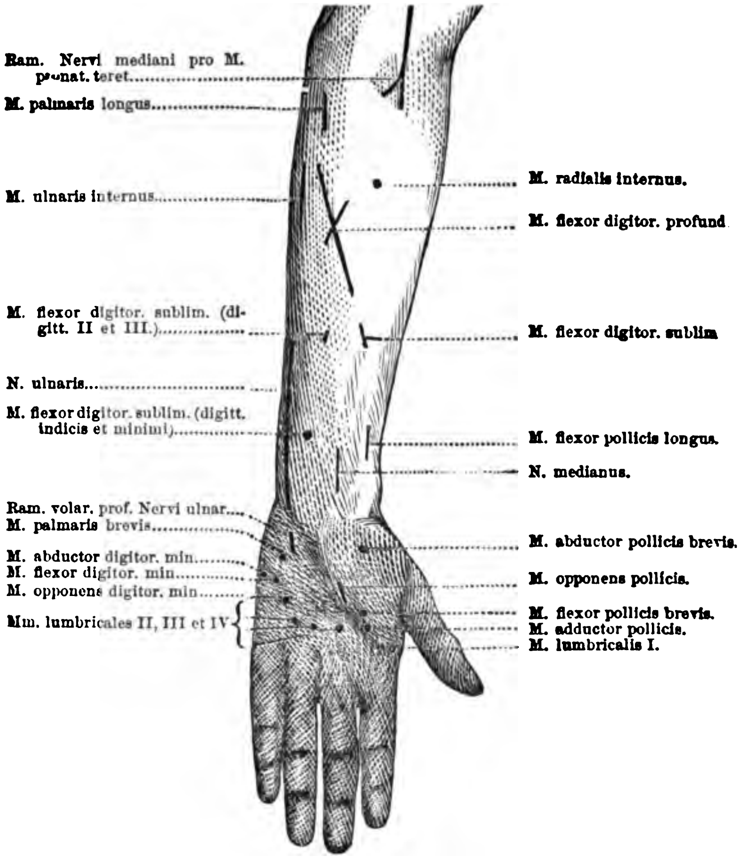

N. cruralis
N. obturatorius
M. sartorius
M. adductor longus
Ram. N. cruralis pro M. quadricipitus.
M. cruralis
Ram. N. cruralis pro M. vasto int.
M. tensor fasciæ lat. (Ram. N glutæi sup.)
M. tensor fasciæ lat. (Ram. N cruralis.)
M. rectus femoris
M. vastus externus.
M. vastus externus.

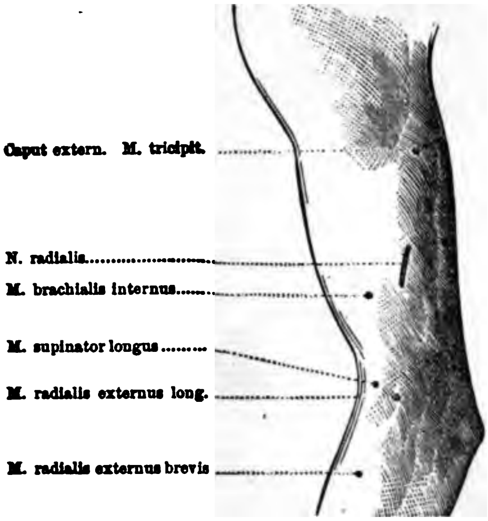

Nerv. peroneus.
M. gastrocnem. externus
M. peroneus longus
M. soleus.
M. tibialis anticus
M. extensor digitor. com
munis longus.
M. peroneus brevis.
M. soleus.
M. flexor hallucis longus
M. extens. halluc. longus
Ram. N. peron. prof. pro M. extens. digitor. brev.
M. extensor digitor. co
munis brevis.
Mm. interossei pedis dorsales.
M. abductor digiti mini
pedis.

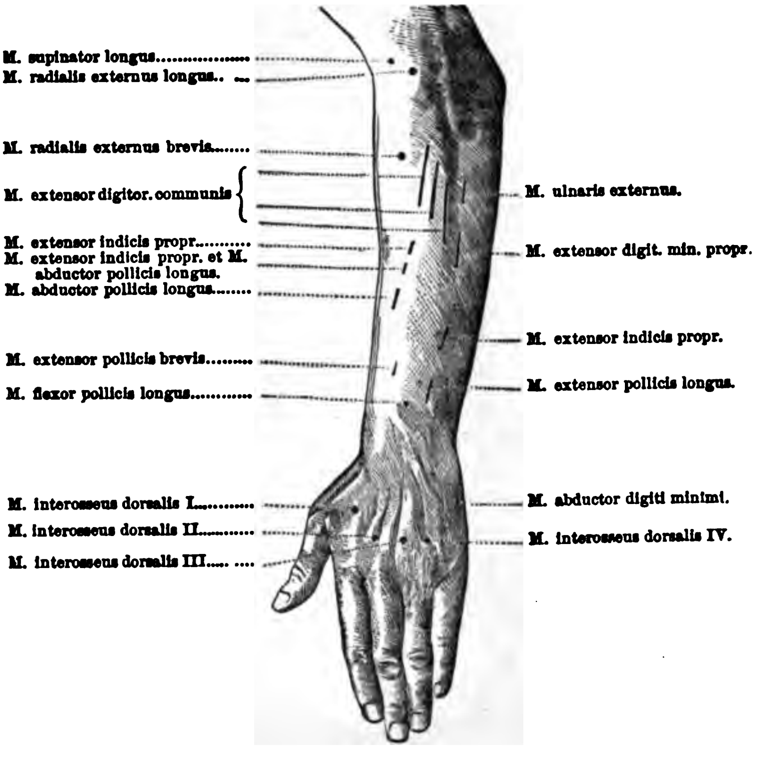

Ram. inf. N. glut. inf. pro M. glut. maximus.
N. ischiadicus.
M. biceps (Caput longum).
M. biceps (Caput breve).
N. tibialis.
N. peroneus.
M. gastrocnemius externus.
M. soleus
M. adductor magnus.
M. semitendinosus.
M. semimembranosus.
M. gastrocnemius internus.


M. gastrocnemius internus.
M. soleus.
M. flexor digitor. communis longus.
N. tibialis.
M. abductor hallucis


N. musculocutaneus.
M. biceps.
N. musculo-cutaneus.
Cap. intern. M. tricipit.
N. medianus.
M. brachialis internus.
N. ulnaris.
Ram. N. mediani pro M. pronator. teret.


Ram. Nervi mediani pro M. pronat. teret
M. palmaris longus
M. ulnaris internus
M. flexor digitor. sublim. (digitt. II et III.)
N. ulnaris
M. flexor digitor. sublim. (digitt. indicis et minimi)
Ram. volar. prof. Nervi ulnar.
M. palmaris brevis
M. abductor digitor. min.
M. flexor digitor. min.
M. opponens digitor. min.
Mm. lumbricales II, III et IV
M. radialis internus.
M. flexor digitor. profund
M. flexor digitor. sublim
M. flexor pollicis longus.
N. medianus.
M. abductor pollicis brevis.
M. opponens pollicis.
M. flexor pollicis brevis.
M. adductor pollicis.
M. lumbricalis I.


Caput extern. M. tricipit.
N. radialis
M. brachialis internus
M. supinator longus
M. radialis externus long.
M. radialis externus brevis


M. supinator longus
M. radialis externus longus
M. radialis externus brevis
M. extensor digitor. communis
M. extensor indicis propr.
M. extensor indicis propr. et M. abductor pollicis longus.
M. abductor pollicis longus
M. extensor pollicis brevis
M. flexor pollicis longus
M. interosseus dorsalis I.
M. interosseus dorsalis II.
M. interosseus dorsalis III.
M. ulnaris externus.
M. extensor digit. min. propr.
M. extensor indicis propr.
M. extensor pollicis longus.
M. abductor digiti minimi.
M. interosseus dorsalis IV.

GENERAL INDEX.

A.

- Absorbents, 661.
- Abstract of aconite, 195.
  - of belladonna, 296.
  - of conium, 406.
  - of digitalis, 158.
  - of ignatia, 341.
  - of jalapa, 512.
  - of nux vomica, 326.
  - of seneka, 577.
- Acacia, 625.
- Aceta, 18.
- Acetate of ammonium, 566.
  - of copper, 49.
  - of lead, 42.
  - of morphine, 255.
  - of potassium, 534.
  - of sodium, 645.
  - of zinc, 46.
- Acetated tincture of opium, 255.
- Acetic acid, 210.
- Acetum, 210.
  - lobeliæ, 392.
  - opii, 255.
  - sanguinariæ, 477.
  - scillæ, 525.
- Acid, benzoic, 578.
  - carbazotic, 86.
  - copaivic, 548.
  - cubebic, 550.
  - gentisic, 59.
  - hydrobromic, 367.
  - meconic, 263.
  - nitrate of mercury, 623.
  - oxalate of potassium, 211.
  - picric, 86.
  - salicylic, 689.
- Acidum aceticum, 210.
  - aceticum dilutum, 210.
  - aceticum glaciale, 210.
  - arseniosum, 409.
  - benzoicum, 578.
  - boricum, 673.
  - carbolicum, 676.
  - carbolicum crudum, 676.
  - chromicum, 624.
  - citricum, 208.
  - gallicum, 29.
  - glaciale, 210.
- Acidum hydrobromicum dilutum, 367.
  - hydrochloricum, 107.
  - hydrochloricum dilutum, 108.
  - hydrocyanicum, 196.
  - hydrocyanicum dilutum, 196.
  - lacticum, 111.
  - muriaticum, 107, 623.
  - muriaticum dilutum, 108.
  - nitricum, 108, 623.
  - nitricum dilutum, 109.
  - nitro-hydrochloricum, 109.
  - nitromuriaticum, 109.
  - nitromuriaticum dilutum, 111.
  - nitrosum, 109.
  - oxalicum, 211.
  - phosphoricum dilutum, 453.
  - picrum, 86.
  - salicylicum, 689.
  - sulphuricum, 105, 623.
  - sulphuricum aromaticum, 107.
  - sulphuricum dilutum, 107.
  - sulphurosum, 675.
  - tannicum, 26.
  - tartaricum, 207.
  - valerianicum, 214.
- Aconella, 185.
- Aconite leaves, 185.
  - as a diaphoretic, 559.
  - root, 185.
- Aconitine, 194, 195.
  - crystallized, 193.
- Aconitum, 184.
  - antidote for, 195.
- Adeps, 31.
  - benzoinatus, 581.
- Adhesive plaster, 40, 140.
- Administration, methods of, 20.
- Æther, 310.
  - fortior, 310.
- African pepper, 92.
- Age, in relation to dose, 22.
- Alcohol, 126.
  - as a sudorific, 567.
- Alcohol dilutum, 126.
  - fortius, 126.
- Alexandria senna, 507.
- Alkalies, 641.
- Allium, 582.
- Allspice, 90.
- Aloe, 504.
  - Barbadensis, 505.
  - Capensis, 505.
  - purificata, 507.
  - Socotrina, 505.
- Aloin, 505.
- Alteratives, 408.
- Althæa, 628.
- Alum, 32.
  - as an emetic, 482.
  - curd, 34.
- Alumen, 32.
  - exsiccatum, 32.
  - sulphas, 34.
- Amber, 220.
- American hellebore, 169.
  - hemp, 263.
- Ammonia, 122, 641.
- Ammonia-alum, 32.
- Ammoniac, 577.
  - mixture, 577.
  - plaster, 577.
- Ammoniacum, 577.
- Ammoniated copper, 48.
  - mercury, 437.
  - tincture of guaiac, 467.
  - tincture of valerian, 214.
- Ammonii acetas, 566.
  - bromidum, 364.
  - carbonas, 126.
  - chloridum, 573.
  - nitras, 126.
  - sulphas, 126.
  - valerianas, 214.
- Ammonio-citrate of bismuth, 45.
- Ammonio-ferric alum, 104, 126.
- Amorphous hyoscyamine, 298.
- Amygdalin, 62.
- Amyl, nitrite of, 381.
  - valerianate of, 391.
- Amyli nitritum, 381.
- Amylic alcohol, 381.
- Anæsthetics, 302.

- Analectronous, 690.
- Analgesics, 240.
- Animal charcoal, 661.
  - quinoidin, 80.
- Anise, 93.
  - water, 93.
- Anisum, 93.
- Anodes, 718.
- Antacids, 641.
- Anthelmintics, 648.
- Anthemis, 89.
- Antihydropin, 542.
- Antimonial ointment, 169.
  - plaster, 169.
  - wine, 169.
- Antimonii et potassii tartras, 163.
  - oxidum, 163.
  - sulphidum, 163.
    - purificatum, 163.
  - sulphuretum, 163.
- Antimony, 163.
- Antipyrin, 701.
- Antiseptics, 663.
- Antispasmodics, 212.
- Apiin, 586.
- Apiol, 586.
- Apomorphine, 477.
- Aquæ ammoniæ, 126, 618.
  - ammoniæ fort., 126, 618.
  - chlori, 670.
  - camphoræ, 218.
  - cinnamomi, 90.
- Aquæ, 18.
- Arabin, 626.
- Araroba, 503.
- Arbuten, 544.
- Argel, 507.
- Argenti cyanidum, 57, 206.
  - iodidum, 57.
  - nitras, 49.
  - nitras dilutus, 57.
  - nitras fucus, 49.
  - oxidum, 57.
- Argentum, 49.
- Argol, 207.
- Argyria, 51, 56.
- Arnica flowers, 177.
  - root, 177.
- Arnicina, 177.
- Aromatic bitters, 88.
  - powder, 90.
  - spirit of ammonia, 126.
  - sulphuric acid, 107.
  - syrup of rhubarb, 504.
  - tincture of rhubarb, 504.
- Aromatics, 88.
  - true, 89.
- Arrow-root, 629.
- Arseniate of sodium, 423.
- Arsenic, 409.
  - antidotes for, 422.
  - as a caustic, 621.
  - eating, 414.
- Arsenical paper, compound, 420.
  - paste, 621.
- Arsenici iodidum, 423.
- Arsenious acid, 409.
- Arsenious ointment, 621.
- Arsenite of potassium, 423.
- Artificial camphor, 141.
- Asafetida, 214.
- Asiatic pill, 394.
- Aspic, 94.
- Aspidium, 654.
- Assafœtida, 214.
  - mixture, 215.
- Astley Cooper's arsenious paste, 621.
- Astringents, 25.
  - mineral, 32.
  - vegetable, 26.
- Atomization, 21, 569.
- Atropine, 296.
  - antagonism to Calabar bean, 354.
  - antagonism to jaborandi, 565.
- Atropinæ sulphas, 296.
- Aurantii amari cortex, 93.
  - dulcis cortex, 93.
  - flores, 93.
- Azedarach, 649.

B.

- Balm, 89.
- Balsam of Peru, 581.
  - of tolu, 581.
- Balsamum Peruvianum, 581.
  - Tolutanum, 581.
  - traumaticum, 581.
- Banks oil, 448.
- Barbadoes aloes, 505.
- Barberry, 61.
- Bark of pomegranate root, 654.
- Barley, 630.
  - water, 630.
- Barytina, 178.
- Bassorin, 626.
- Baths, cold, 707.
  - hot, 553, 667.
  - Turkish, 553.
  - vapor, 553.
- Bean of St. Ignatius, 341.
- Bearberry, 544.
- Bebeerine, 60.
  - sulphate, 60.
- Bebeeru bark, 60.
- Belladonna in opium-poisoning, 289.
  - leaves, 269.
  - plaster, 270.
  - root, 269.
- Belladonnæ folium, 269.
  - radix, 269.
- Benzoic acid, 578.
- Benzoin, 577.
- Benzoinum, 577.
- Berberine, 61, 514.
- Berberis, 61.
- Bicarbonate of potassium, 534.
  - of sodium, 644.
- Bichloride of mercury, 434.
- Bichloride of methylene, 324.
- Biniodide of mercury, 436.
- Bismuth, 44.
- Bismuthi citras, 45.
  - et ammonii citras, 45.
  - subcarbonas, 44.
  - subnitras, 44.
- Bismuthum, 44.
- Bisulphate of quinine, 84.
- Bitartrate of potassium, 534.
- Bitter orange peel, 93.
- Bitters, peculiar, 62.
  - simple, 56.
- Black draught, 507.
  - drop, 255.
  - ginger, 91.
  - hellebore, 585.
  - mustard, 616.
  - oak, 31.
  - oil, 448.
  - oxide of manganese, 104.
  - pepper, 91.
  - snakeroot, 222.
  - wash, 437.
- Blackberry, 32.
- Blatta orientalis, 542.
- Blattic acid, 542.
- Bleaching powder, 672.
- Blistering cerate, 614.
- Blisters, 610, 614.
- Bloodroot, 476.
- Blue galls, 30.
  - mass, 432, 500.
  - ointment, 432, 500.
  - pills, 432, 500.
- Bluestone, 47.
- Boneblack, 661.
- Boneset, 61.
- Bonwill's method of anæsthesia, 304.
- Boracic acid, 673.
- Borax, 673.
- Boric acid, 673.
- Bougies, 21.
- Bran, 493.
- Brandy, 126.
- Brayera, 650.
- Brazilian sarsaparilla, 463.
- Bromal hydrate, 367.
- Bromated camphor, 218.
- Bromcamphor, 219.
- Bromide of ammonium, 364.
  - of camphor, 218.
  - of ethyl, 325.
  - of iron, 104.
  - of lithium, 366.
  - of potassium, 356.
  - of quinine, 84.
  - of sodium, 366.
- Brominated camphor, 219.
- Bromine, 624, 671.
- Bromoform, 325.
- Bromum, 624, 671.
- Broom, 528.
- Brown mixture, 628.
  - oil, 448.
  - sugar, 493.
- Brucine, 341.

Buchu, 543.
Buckthorn, 495.
Burgundy pitch, 618.
  pitch plaster, 618.
Burnt alum, 34, 624.
Butternut, 504.
Butyl chloral hydrate, 380.
Buxia, 60.

C.

Cacao butter, 631.
Cadmii sulphas, 47.
Cadmium, 47.
Caffea, 223.
Caffeine, 223.
Calabar bean, 342.
Calabarina, 342.
Calabarinum purum (footnote), 342.
Calamine, 46.
Calamus, 94.
Calcii carbonas præcipitata, 646.
Calcii phosphas præcipitatus, 453.
California buckthorn, 495.
Calisaya bark, 64.
Calomel, 433.
  as a purge, 500.
Caloric, 704.
Calumba, 61.
Calx, 645.
  chlorata, 672.
  sulphurata, 498.
Camboge, 517.
Camphor, 215.
Camphor, artificial, 141.
  bromated, 218.
  carbolated, 219.
  cymol, 216.
  mixture, Hope's, 219.
  monobromate of, 218.
  oil, 215, 218.
  water, 218.
Camphora, 215.
Camphorated tincture of opium, 254.
Canada balsam, 546.
  erigeron, 546.
  fleabane, 546.
  pitch, 618.
  pitch plaster, 618.
  turpentine, 546.
Canna, 630.
Cannabin, 263.
Cannabis Americana, 263.
  Indica, 263.
Canquoin's paste, 622.
Cantharidal collodion, 614.
Cantharides, 587, 611.
  cerate, 614.
  paper, 614.
Cantharidin, 611.
Cantharis, 552.
Cape aloes, 505.
Capsicin, 92.
Capsicum, 92.
Caraway, 93.
Carbazotate of ammonium, 87.
Carbazotic acid, 86.
Carbo, 661.
  animalis, 661.
  animalis purificatus, 661.
  ligni, 661.
Carbolated camphor, 219.
Carbolic acid, 676.
  antidote to, 687.
  as an antiseptic, 688.
  parenchymatous injections of, 684.
  poisoning, 685.
Carbonate of ammonium, 126.
  of calcium, 646.
  of lead, 43.
  of lithium, 542.
  of magnesium, 495.
  of potassium, 534.
  of sodium, 644.
  of zinc, 46.
Cardamom, 90.
Cardamomum, 90.
Cardiac sedatives, 162.
  stimulants, 122.
Carminatives, 88.
Carolina jessamine, 392.
Carrageen, 627.
Carrageenin, 627.
Carron oil, 646.
Carthagena bark, 64.
Carum, 93.
Caryophyllus, 90.
Cascara Sagrada, 495.
Cascarilla, 89.
Cassava, 628.
Cassia bark, 90.
  fistula, 495.
Castillon's powder, 646.
Castor, 213.
  oil, 498.
  oil beans, 498.
Castoreum, 213.
Catechu, 30.
Cathartic acid, 507.
Cathartics, 483.
Cathartine, 507.
Cathode, 718.
Caustic potash, 620.
  soda, 644.
Cayenne pepper, 92.
Central galvanization, 741.
Cera alba, 632.
  flava, 632.
Cerata, 19.
Cerates, 19.
Ceratum cantharidis, 614.
  extracti cantharidis, 614.
Cerebrum, galvanization of, 735.
Cerii oxalas, 45.
Cetaceum, 631.
Cetraria, 626.
Cetraric acid, 627.
Cetrarin, 627.
Chalk, 646.
Chalk mixture, 647.
Chamomile, 89.
Champagne, 139.
Charcoal, 661.
  poultices, 661.
Charta arsenicalis composita, 420.
  cantharidis, 614
  sinapis, 617.
Chartæ, 19.
Chelerythrin, 476.
Chemical current, 685.
  food, 456.
Chenopodium, 649.
Chian turpentine, 143.
Chili saltpetre, 537.
Chimaphila, 545.
Chimaphilin, 545.
Chinoidin, 86.
Chinoidinum, 86.
Chiretta, 62.
Chloral, 368.
  alcoholate, 368.
  camphor, 379.
  hydrate, 368.
  poisoning, 378.
Chlorate of potassium, 539.
  of sodium, 541.
Chloride of ammonium, 574.
  of iron, 102.
  of mercury, corrosive, 433.
  of mercury, mild, 433.
  of potassium, 433.
  of zinc, 622.
Chlorinated lime, 672.
Chlorine, 670.
  water, 670.
Chlorum, 670.
Chloroform, 315.
Chloroformum purificatum, 316.
  venale, 316.
Cholagogues, 488.
Chondrus, 627.
Chromic acid, 624.
Chrysaroba, 503.
Chrysophanic acid, 503.
Churrus, 263.
Cigarettes, arsenical, 420.
Cimicifuga, 222.
Cinchona, 63.
  flava, 64.
  pale, 63.
  pallida, 63.
  red, 64.
  rubra, 64.
  yellow, 64.
Cinchonidine, 85.
Cinchoninæ sulphas, 85.
Cinchonine, 85.
  sulphate of, 85.
Cinchonism, 66.
Cinnamic acid, 581.
Cinnamon, 89.
  water, 90.
Citrate of bismuth, 45.
  of bismuth and ammonium, 45.
  of iron, 103.

Citrate of iron and ammonium, 104.
    of iron and quinine, 104.
    of iron and strychnine, 104.
    of lithium, 542.
    of potassium, 534, 559.
Citric acid, 205.
Classification, 24.
Climate, 21.
Cloves, 90.
Clove-tea, 90.
Coca, 231.
Cocaine, 231.
Coca-tannic acid, 231.
Cockroach, 512.
Codeine, 258.
Cod-liver oil, 448.
Coffee, 223.
Cohnheim's salt frog, 373.
Cola nut, 223.
Colchiceine, 456.
Colchici radix, 456.
    semen, 456.
Colchicine, 456.
Colchicum root, 456.
    seed, 456.
Cold as a tonic, 707.
    in pyrexia, 705.
    local use of, 705.
Cold cream, 632.
Collodion, 638.
    with cantharides, 614.
Collodium, 638.
Collodium cum cantharide, 614.
    flexile, 639.
Colocynth, 512.
Colocynthin, 512.
Colocynthis, 512.
Columbin, 61.
Columbo, 61.
Commercial bicarbonate of sodium, 644.
    chloroform, 316.
    oxide of zinc, 46.
Compound arsenical paper, 420.
    cathartic pills, 514.
    decoction of sarsaparilla, 464.
    extract of colocynth, 513.
    fluid extract of sarsaparilla, 464.
    infusion of flaxseed, 628.
    infusion of gentian, 60.
    infusion of rose, 32.
    iodine ointment, 444.
    jalap powder, 512.
    liquorice powder, 508.
    mixture of iron, 101.
    mixture of liquorice, 628.
    pills of iron, 101.
    pills of rhubarb, 504.
    powder of ipecacuanha, 558.
    powder of jalap, 512.
Compound powder of rhubarb, 504.
    solution of iodine, 442.
    spirit of ether, 220.
    spirit of juniper, 546.
    spirit of lavender, 89.
    syrup of sarsaparilla, 464.
    syrup of squill, 582.
    syrup of the phosphates, 456.
    tincture of benzoin, 581.
    tincture of cardamom, 91.
    tincture of catechu, 30.
    tincture of cinchona, 86.
    tincture of gentian, 60.
    tincture of iodine, 442.
Confection of rose, 32.
    of senna, 508.
Confectiones, 18.
Confections, 18.
Conia, 402.
Conii folia, 401.
    fructus, 401.
Continuous current, 722.
Convallamarin, 159.
Convallaria majalis, 159.
Convallarin, 159.
Cooper's arsenious ointment, 621.
Copaiba, 548.
Copaivic acid, 548.
Copper, 47.
Copperas, 667.
Coptis, 62.
Coriander, 93.
Coriandrum, 93.
Cornus Florida, 60.
Corrosive chloride of mercury, 433.
    sublimate, 434, 668.
        as a caustic, 623.
Corsican moss, 627.
Cotton root, 604.
Counter-irritation, 607.
Cowhage, 655.
Coxe's hive syrup, 582.
Cranesbill, 32.
Cream of tartar, 536.
Creasote, 677.
Creasotum, 677.
Creta, 646.
    præparata, 646.
Croton choral hydrate, 380.
Croton oil, 488, 519.
Crotonol, 519.
Cryptopia, 262.
Cubeb, 550.
Cubeba, 550.
Cubebic acid, 550.
Cubebin, 550.
Cupri acetas, 50.
    sulphas, 47.
Cuprum, 47.
    ammoniatum, 50.
Cyanide of potassium, 6.
    of silver, 57, 206.
Cyano-hæmoglobin, 199.
Cyanogen gas, 206.
Cydonium, 628.
Cytisin, 177.

D.

Dandelion, 466.
Daphnin, 465.
Daturine, 296.
Decocta, 17.
Decoction of barley, 630.
Decoctum chimaphilæ, 545.
    sarsaparillæ compositum, 464.
Degeneration, reaction of, 729.
Demulcents, 625.
Denarcotized opium, 255.
Deodorized tincture of opium, 255.
Depresso-motors, 342.
Dewee's emmenagogue mixture, 586.
Dextro-quinia, 85.
Diagnosis, use of electricity in, 731.
Dialyzed iron, 103.
Diaphoretics, 553.
Digestants, 656.
Digitalein, 144.
Digitalin, 143, 159.
Digitalinum, 143, 159.
Digitaliresin, 144.
Digitalis, 143.
    as an antipyretic, 156.
    as a diuretic, 525.
Digitonin, 144.
Digitoxin, 144.
Dihydroxyle quinine, 77.
Diluents, 637.
Diluted acetic acid, 210.
    alcohol, 126.
    hydrobromic acid, 367.
    hydrocyanic acid, 196.
    muriatic acid, 108.
    nitric acid, 109.
    nitromuriatic acid, 108.
    phosphoric acid, 453.
    solution of subacetate of lead, 41.
    sulphuric acid, 107.
Diospyros, 32.
Disinfectants, 663.
Diuretics, 521.
Dogwood, 62.
Donovan's solution, 423, 444.
Doses, rules for, 22.
Dover's powder, 558.
Drastics, 511.
Dried alum, 32.
    carbonate of sodium, 644.
    sulphate of iron, 97.

E.

Echolina, 590.
Effects of medicines, primary, 19.

- Effects of medicines, remote, 19.
- Effervescing draught, 584, 559.
- Egg-nogg, 40.
- Elaterin, 516.
- Elaterium, 515.
- Electric brush, 728.
- Electricity, 718.
  - use of, as a tonic, 738.
- Elixir Proprietatis, 507.
  - of valerianate of ammonium, 214.
  - of vitriol, 107.
- Emetics, 467.
  - mineral, 482.
  - vegetable, 471.
- Emetine, 471.
- Emmenagogues, 584.
- Emodin, 495.
- Emollients, 631.
- Emplastra, 19.
- Emplastrum ammoniaci, 577.
  - ammoniaci cum hydrargyro, 577.
  - antimonii, 161.
  - asafœtidæ, 215.
  - belladonnæ, 270.
  - hydrargyri, 432.
  - picis Burgundicæ, 618.
  - picis Canadensis, 618.
  - picis cum cantharide, 618.
  - plumbi, 42, 638.
  - resinæ, 42, 140, 638.
  - saponis, 42, 638.
- Emulsin, 62, 616.
- Emulsions, 18.
- Endermic administration, 21.
- Enemata, 490.
- English aconitia, 185.
  - garlic, 582.
- Epispastics, 607, 610.
- Epsom salt, 508.
- Ergot, 589.
- Ergota, 589.
- Ergotic acid, 590.
- Ergotin, 603.
- Ergotine, 590.
- Ergotinine, 590.
- Ergotism, 601.
- Erigeron, 546.
  - Canadense, 546.
- Errhines, 606.
- Erythroxyline, 231.
- Erythroxylon, 231.
- Escharotics, 619.
- Eserine, 342.
- Essence of peppermint, 94.
  - of spearmint, 94.
- Essential salt of lemons, 211.
- Ether, 310.
- Ethereal oil, 220.
- Ethyl, lead, 40.
  - nitrite of, 391.
  - oxide, 310.
- Eucalypsinthe (foot-note), 94.
- Eucalyptus, 94.
- Euonymin, 508.
- Euonymus, 508.
- Eupatorium, 61.
- Excito-motors, 326.
- Expectorants, 569.
- Extract of aconite, 195.
  - of American hemp, 248.
  - of arnica, 178.
  - of belladonna, 296.
  - of black hellebore, 490.
  - of butternut, 504.
  - of Calabar bean, 353.
  - of chiretta, 62.
  - of cinchona, 86.
  - of colchicum root, 462.
  - of colocynth, 513.
  - of conium, 406.
  - of dandelion, 466.
  - of digitalis, 158.
  - of ergot, 604.
  - of euonymus, 478.
  - of gentian, 60.
  - of hæmatoxylon, 31.
  - of hellebore, 520.
  - of hyoscyamus, 299.
  - of ignatia, 341.
  - of Indian hemp, 263.
  - of krameria, 31.
  - of liquorice, 628.
  - of logwood, 31.
  - of May-apple, 515.
  - of nux vomica, 326.
  - of opium, 254.
  - of podophyllum, 515.
  - of quassia, 59.
  - of rhatany, 31.
  - of rhubarb, 504.
  - of stramonium, 297.
  - of taraxacum, 466.
  - of uva ursi, 545.
  - of wahoo, 508.
- Extracta, 18.
  - fluida, 18.
- Extractum cannabis Indicæ, 263.
  - hæmatoxyli, 31.
  - juglandis, 504.

F.

- Faradic current, 722.
- Faradization, general, 740.
- Feeding by the rectum, 659.
- Fennel, 93.
  - water, 93.
- Ferri carbonas saccharatus, 101.
  - chloridum, 102.
  - citras, 103.
  - et ammonii citras, 104.
  - et ammonii sulphas, 104.
  - et ammonii tartras, 104.
  - et potassii tartras, 104.
  - et quininæ citras, 104.
- Ferri et strychninæ citras, 104.
  - lactas, 104.
  - oxidum hydratum, 100.
  - oxidum hydratum cum magnesia, 101.
  - phosphas, 104.
  - pulvis, 100.
  - pyrophosphas, 104.
  - subcarbonas, 100.
  - sulphas, 101.
  - sulphas exsiccata, 102.
  - sulphas præcipitatus, 102.
- Ferrum, 97.
  - dialysatum, 103.
  - reductum, 100.
- Figs, 494.
- Filix mas, 654.
- Flaxseed, 628.
  - meal, 628.
  - oil, 628.
- Fleabane, 546.
- Fleming's tincture of aconite, 195.
- Flexible collodion, 639.
- Flowers of sulphur, 496.
- Fluid extract of aconite root, 195.
  - of American hellebore, 176.
  - of arnica, 178.
  - of belladonna, 296.
  - of bitter orange peel, 93.
  - of boneset, 62.
  - of brayera, 650.
  - of buchu, 543.
  - of chimaphila, 544.
  - of chiretta, 62.
  - of cimicifuga, 223.
  - of cinchonæ, 86.
  - of colchicum root, 462.
  - of colchicum seeds, 462.
  - of columbo, 61.
  - of conium seed, 406.
  - of cotton root, 604.
  - of cubebs, 552.
  - of dandelion, 466.
  - of digitalis, 158.
  - of ergot, 603.
  - of eucalyptus, 97.
  - of eupatorium, 62.
  - of gelsemium, 396.
  - of gentian, 60.
  - of ginger, 91.
  - of hemp, 268.
  - of hops, 221.
  - of ipecacuanha, 476.
  - of jaborandi, 565.
  - of krameria, 31.
  - of lactucarium, 222.
  - of lemon peel, 93.
  - of liquorice, 628.
  - of lobelia, 392.
  - of lupulin, 221.
  - of matico, 552.
  - of nux vomica, 326.
  - of pareira brava, 544.
  - of quassia, 59.

Fluid extract of rhatany, 31.
  of rhubarb, 504.
  of sanguinaria, 477.
  of sarsaparilla, 464.
  of seneka, 577.
  of senna, 508.
  of serpentaria, 89.
  of spigelia, 649.
  of spigelia and senna, 649.
  of squill, 525.
  of stramonium, 297.
  of sumach, 32.
  of sweet orange peel, 93.
  of taraxacum, 466.
  of uva ursi, 545.
  of valerian, 214.
  of veratrum viride, 176.
  of wild cherry, 63.
Fœniculum, 93.
Foot-bath, method for, 567.
Forced injections, 490.
Forces, 701.
Fowler's solution, 423.
Frangula, 495.
Franguline, 495.
Frère Cosme, arsenical paste of, 621.
Fumigations, mercurial, 431.
Fusel oil, 381.

G.

Gaduin, 449.
Galactagogue, 499.
Galla, 30.
Gallic acid, 29.
Gallo-tannic acid, 26.
Galls, 30.
Galvanic current, 719.
Gambir, 30.
Gamboge, 517.
Gambogia, 517.
Gambogic acid, 518.
Garlic, 582.
Gas liquor, 574.
Gaultheria, 94.
Gelsemine, 393.
Gelseminic acid, 393.
Gelsemium, 392.
General faradization, 740.
Gentian, 59.
Gentiana, 59.
Gentiopikrin, 60.
Gentisic acid, 59.
Geranium, 32.
German aconitine, 185.
  chamomile, 89.
Germicide, 663.
Gin, 546.
Ginger, 91.
Gizzard, 656.
Glacial acetic acid, 210.
Glauber salt, 509.
Glycerine, 632.
Glycerinum, 632.
Glycerita, 18.
Glycerite of egg, 635.
Glycerite of gallic acid, 29.
  of starch, 635.
  of tannic acid, 29.
Glycyrrhiza, 627.
Glycyrrhizin, 627.
  ammoniatum, 628.
Goa powder, 503.
Goldthread, 62.
Goose-grease, 631.
Gossypii radicis cortex, 604.
Goulard's extract, 43.
Granati fructus cortex, 32, 654.
  radicis cortex, 32, 654.
Granatum, 654.
Granulated citrate of magnesium, 509.
Gray powder, 432.
Green galls, 30.
  ginger, 91.
  iodide of mercury, 436.
Guaiac, 464.
  acid, 465.
  as an emmenagogue, 587.
Guaiac-yellow, 465.
Guaiaci lignum, 464.
  resina, 464.
Guaiacic acid, 465.
Guaiacin, 465.
Guaiaconic acid, 465.
Guaiacresinic acid, 465.
Guaiacum wood, 464.
Guarana, 223.
Gum arabic, 625.
Gun cotton, 638.
Gunjah, 263.
Gutta-percha, 640.

H.

Habit, 22.
Hæmatin, 31.
Hæmatoxylin, 31.
Hæmatoxylon, 31.
Hartshorn, spirit of, 126.
Hashish, 263.
Heat, 665, 704.
Heavy magnesia, 495.
  oil of wine, 220.
Helleboreine, 520.
Helleborine, 520.
Helleborus, 520.
Hemlock pitch, 618.
  plaster, 618.
Hemp, 263.
Herapathite, 65.
Hippuric acid, 579.
Hive syrup, 582.
Hoffmann's anodyne, 220.
Honduras sarsaparilla, 463.
Honey, 18.
Hop poultice, 221.
Hope's camphor mixture, 108.
Hops, 220.
Hordeum, 630.
Hot baths, 554.
Humulus, 220.
Huxham's tincture, 86.
Hydragogue diuretics, 523.
Hydragogues, 489.
Hydrargyrum, 424.
  ammoniatum, 437.
  chloridum corrosivum, 434.
  chloridum mite, 433.
  cum creta, 432.
  iodidum rubrum, 436.
  iodidum viride, 436.
  oleatum, 432.
  oxidum flavum, 436.
  oxidum rubrum, 436.
  sulphas flavus, 436.
  sulphidum rubrum, 436.
Hydrate of chloral, 368.
Hydrated oxide of iron, 100.
  sesquioxide of iron, 100.
Hydriodate of hyoscine, 301.
Hydrobromate of conine, 406.
  of homatropine, 296.
  of hyoscine, 301.
  of quinine, 84.
Hydrobromic acid, 367.
Hydrochinone, 544.
Hydrochlorate apomorphine, 477.
  of morphine, 255.
Hydrochloric acid, 107.
Hydrocotarnine, 263.
Hydrocyanic acid, 196.
Hyoscine, 263.
Hyoscyami folia, 298.
  semen, 298, 300.
Hyoscyamine, 298.
Hyoscyaminæ sulphas, 298.
Hyoscyamus leaves, 298.
  seed, 298, 300.
Hyperemesis, 470.
Hypochlorites, 672.
Hypodermic injections, 20.
  injections of calomel, 434.

I.

Iceland moss, 626.
Idiosyncrasies, 22.
Igasuric acid, 326.
Ignatine, 341.
Ilex, 223.
Incompatibilities, 745.
Indian corn, 546.
Indian hemp, 263.
Indian meal, 493.
  smut of, 604.
  stigmata of, 546.
Indian senna, 507.
Indications for the use of medicines, 19.
Induced current, 722.
Infusa, 18.
Infusion of brayera, 650.
  of buchu, 543.
  of capsicum, 92.
  of cascarilla, 89.
  of chamomile, 89.

Infusion of cinchona, 86.
  of cloves, 90.
  of digitalis, 158.
  of gentian compound, 60.
  of ginger, 91.
  of hops, 321.
  of juniper, 546.
  of krameria, 31.
  of pareira brava, 544.
  of quassia, 59.
  of rhatany, 31.
  of senna, 508.
  of valerian, 213.
  of wild cherry, 63.
Infusum picis liquidæ, 583.
Inunctions, mercurial, 431.
Iodide of arsenic, 423.
  of potassium, 442.
  of silver, 57.
Iodine, 437.
  ointment, 442.
Iodism, 439.
Iodoform, 444.
  ointment, 447.
Iodoformum, 444.
Iodum, 437.
Ipecacuanha, 471.
  as a diaphoretic, 558, 573.
  as an expectorant, 573.
Irish moss, 627.
Iron, 97.
  by hydrogen, 100.
  Quevenne's, 100.
Iron rust, 100.
Isopelletierine, 655.

J.

Jaborandi, 559.
  antagonism to atropia, 565.
Jaborine, 559.
Jaguarandy, 559.
Jalap, 511.
Jalapa, 511.
Jamaica ginger, 91.
Jamestown weed, 296.
Jamguarandi, 559.
Jamgurandy, 559.
Jervine, 170, 176.
Juglans, 504.
Juice of conium, 406.
Juices, 18.
Juniper, 545.
Juniperus, 545.

K.

Kairin, 703.
Kamala, 655.
Kameela, 655.
Katalectronous, 729.
Kentish ointment, 618.
Kinic acid, 64.
Kino, 30.
Kino-tannic acid, 26.
Kinovic acid, 64.
Kola nut, 223.
Koossin, 650.
Kousso, 650.
Krameria, 31.

L.

Labarraque's solution, 673.
Lactate of iron, 104.
Lactic acid, 111.
Lacto-phosphate of lime, 455.
Lactucarium, ~~211~~. 221
Lactucin, 211.
Lady Webster pills, 507.
Lard, 631.
Laudanine, 262.
Laudanum, 255.
  deodorized, 255.
Lavandula, 93.
Lavender, 93.
Laxatives, 493.
Lead, 34, 666.
  acetate of, 42.
  carbonate of, 43.
  ethyl, 40.
  nitrate of, 43.
  oxide of, 42.
  plaster, 42, 638.
  poisoning, 35.
  water, 43.
Ledoyen's disinfectant solution, 43, 666.
Lemon-juice, 209.
Lemon peel, 93.
Lemons, essential salt of, 211.
Levant wormseed, 650.
Lichen starch, 627.
Lichenin, 627.
Lichstearic acid, 627.
Light magnesia, 495.
Lignum-vitæ, 464.
Lily of the valley, 159.
Lime, 645.
  as a disinfectant, 668.
  juice, 209.
  lacto-phosphate of, 456.
  liniment, 645.
  water, 645.
Limonis cortex, 93.
Lini farina, 628.
Liniment of ammonia, 618.
  of camphor, 218.
  of cantharides, 614.
  of chloroform, 324.
  of lime, 645.
  of soap, 218.
  of turpentine, 618.
Linimenta, 19.
Linimentum calcis, 645.
  camphoræ, 218.
  cantharidis, 614.
  chloroformi, 324.
  saponis, 218.
  terebinthinæ, 618.
Linum, 628.
Liquor acidi arseniosi, 423.
  ammonii acetatis, 566.
Liquor arsenici et hydrargyri, iodidi, 444.
  bismuthi et ammonii, citratis, 43.
  calcis, 645.
  ferri chloridi, 102.
  ferri subsulphatis, 102.
  ferri tersulphatis, 102.
  gutta-perchæ, 640.
  hydrargyri nitratis, 623.
  iodi compositus, 442.
  magnesii citratis, 509.
  morphiæ sulphatis, 255.
  pancreaticus, 658.
  plumbi subacetatis, 41.
  plumbi subacetatis dilutus, 42.
  potassæ, 642.
  potassii arsenitis, 423.
  potassii citratis, 534.
  potassii permanganatis, 670.
  sodæ, 644.
  sodæ chlorinatæ, 673.
  sodii arseniatis, 423.
  zinci chloridi, 623.
Liquores, 18.
Liquorice, 628.
  root, 627.
Lisbon diet-drink, 464.
Litharge, 42.
Lithii carbonas, 542.
Lithium, bromide of, 366.
Liver, action of cathartics on, 488.
Lobelia, 391, 573.
Lobelic acid, 391, 573.
Lobeline, 391.
Logwood, 31.
Lozenges of cubebs, 573.
  of ipecacuanha, 573.
  of ipecacuanha and morphia, 573.
  of santonin, 573.
Lugol's solution, 442.
Lunar caustic, 48.
Lupulin, 211.
Lupulina, 211.
Lycotonine, 184.

M.

Mace, 90.
Macis, 90.
Magendie's solution, 256.
Magnesia, 495.
Magnesia ponderosa, 495.
Magnesii carbonas, 495.
  citras granulatus, 509.
  sulphas, 508.
Maizenic acid, 546.
Male fern, 654.
Malic acid, 32.
Manganese, 104.
  black oxide of, 104.
  sulphate of, 104.
Mangani oxidum nigrum, 104.
  sulphas, 104.

Manna, 494.
Mannite, 494.
Maranta, 629.
Massa copaibæ, 550.
  hydrargyri, 432.
Maté, 223.
Materia medica, 2.
Maticin, 552.
Matico, 552.
Matricaria, 89.
May-apple, 514.
Meadow saffron, 456.
Measures, 740.
Meconic acid, 263.
Meconine, 262.
Medulla sassafras, 628.
Melissa, 93.
Mellita, 18.
Mentha piperita, 93.
  viridis, 93.
Menthol, 94.
Mercurial ointment, 432.
  oleate, 432.
  plaster, 432.
  purgatives, 500.
Mercury, 424, 500.
  ammoniated, 43[illegible].
  hypodermic use of, 437.
  with chalk, [illegible]32.
Metachloral, 379.
Methyl chloride, 315.
Methylene bichloride, 324.
Mezereon, 465.
  ointment, 465.
Mezereum, 465.
Mild chloride of mercury, 433.
Milk of assafetida, 215.
Milk-punch, 139.
Mineral emetics, 482.
  tonics, 97.
Mistura ammoniaci, 577.
  cretæ, 647.
  ferri composita, 101.
  glycyrrhizæ composita, 628.
  potassii citratis, 534.
Misturæ, 18.
Mixture of assafetida, 215.
  of chloroform, 324.
  of citrate of potassium, 534.
Molasses, 493.
Monobromate of camphor, 218.
Monsel's solution, 102.
Morphine, 244, 255.
  and chloral, 250.
Morphinæ acetas, 255.
  hydrochloras, 255.
  murias, 255.
  sulphas, 255.
Moschus, 212.
Motor points, 727.
Mucilage of gum arabic, 626.
  of quince-seed, 627.
  of sassafras pith, 628.
  of slippery-elm bark, 626.
Mucilage of tragacanth, 626.
Mucilagines, 18.
Mucuna, 655.
Mulled wine, 139.
Muriate of ammonia, 574.
  of morphine, 255.
Muriatic acid, 107.
  as a caustic, 624.
Muscaria, antidote for, 158.
Musk, 212.
Mustard, 615.
  as an emetic, 481.
  paper, 617.
  plaster, 616.
Mutton suet, 631.
Mydriasis, 269.
Mydriatics, 269.
Myristica, 90.
Myronic acid, 616.
Myrrh, 584.
Myrrha, 584.

N.

Napelline, 185.
Narceine, 256.
Narcotine, 260.
Nauseating diaphoretics, 558.
Nectandra, 60.
Neutral mixture, 534.
Nicotia, 396.
Nicotianine, 396.
Nitrate of ammonium, 126.
  of lead, 42.
  of mercury, solution of, 623.
  of potassium, 536.
  of silver, 47.
  of sodium, 537.
Nitre, 536.
Nitric acid, 108.
  as a caustic, 623.
Nitrite of amyl, 381.
  of ethyl, 391.
  of potassium, 389.
  of sodium, 389.
Nitrites, action of, on the blood, 385.
Nitrogen monoxide, 305.
Nitroglycerine, 390.
Nitrohydrochloric acid, 109.
Nitromuriatic acid, 109.
Nitrous acid, 108.
  oxide, 305.
Norwood's tincture of veratrum viride, 176.
Nutgall, 30.
Nutmeg, 90.
Nux vomica, 326.

O.

Ohm's law, 719.
Oil of amber, 220.
  of anise, 93.
  of cajeput, 92.
  of camphor, 215, 218.
Oil of caraway, 93.
  of chenopodium, 649.
  of cinnamon, 90.
  of cloves, 90.
  of copaiba, 550.
  of coriander, 93.
  of cubeb, 552.
  of erigeron, 143, 546.
  of eucalyptus, 94, 97.
  of fennel, 93.
  of gaultheria, 94.
  of juniper, 545.
  of lavender, 93.
  of marjoram, 93.
  of mustard, 616.
  of nutmeg, 90.
  of pennyroyal, 588.
  of pepper, 91.
  of peppermint, 94.
  of phosphorus, 121.
  of pimento, 90.
  of rosemary, 93.
  of rue, 586.
  of sassafras, 93, 463.
  of savine, 586.
  of spearmint, 93.
  of succinum, 220.
  of tansy, 586.
  of tar, 582.
  of turpentine, 140, 547.
  of valerian, 213.
  of vitriol, 105.
  of wormseed, 649.
Ointment, 19.
  of ammoniated mercury, 436.
  of antimony, 169.
  of belladonna, 296.
  of carbonate of lead, 43.
  of gallic acid, 29.
  of galls, 30.
  of iodine, 442.
  of mezereon, 465.
  of nutgall, 30.
  of oxide of zinc, 46.
  of red iodide of mercury, 436.
  of rose water, 632.
  of stramonium, 297.
  of tannic acid, 29.
  of veratria, 184.
  of white precipitate, 437.
  of yellow oxide of mercury, 436.
Olea destillata, 18.
Oleate of mercury, 432.
Oleatum veratrinæ, 184.
Oleoresin of black pepper, 92.
  of capsicum, 92.
  of cubeb, 552.
  of fern, 654.
  of ginger, 91.
  of lupulin, 221.
Oleoresinæ, 18.
Oleum æthereum, 220.
  cajuputi, 92.
  chenopodii, 649.
  erigerontis, 546.

Oleum morrhuæ, 448.
  phosphoratum, 121.
  ricini, 498.
  succini, 220.
  terebinthinæ, 140.
  theobromæ, 631.
  tiglii, 519.
Opianine, 263.
Opium, 240.
  alkaloids, 255.
  denarcotization, 254.
  poisoning by, 251.
  Turkey, 240.
Orange flowers, 93.
  flower water, 93.
  peel, 93.
Oxalate of cerium, 45.
  of potassium, 211.
Oxalic acid, 211.
Oxide of antimony, 163.
  of ethyl, 310.
  of iron, hydrated, 100, 666.
  of lead, 42.
  of silver, 57.
  of zinc, 46.
Oxytocics, 589.
Oyster-shell, 646.

P.

Pale catechu, 30.
  cinchona, 63.
  rose, 32.
Pancreatic diastase, 658.
  extracts, 658.
Pancreatin, 658.
Papaverine, 261.
Paraglin, 463.
Paraglinic acid, 463.
Paraguay tea, 221.
Paramorphine, 260.
Paregoric, 254.
Pareira, 543.
  brava, 543.
Parsley, 586.
Pearl ash, 534.
  sago, 629.
Peculiar bitters, 62.
Pelletierine, 655.
Pellitory, 605.
Pelosine, 60.
Pepo, 654.
Peppermint, 93.
  water, 93.
Pepsin, 656.
Pepsina, 656.
Peptonized beef tea, 659.
  gruel, 659.
  milk, 659.
Permanganate of potassium, 669.
Persimmon, 32.
Petroselinum, 586.
Pharmacology, 17.
Pharmacopœia, 17.
Pharmacy, 17.
Phenic acid, 676.
Phenylic alcohol, 676.
Phosphate of calcium, 454.
  of iron, 104.
  of sodium, 510.
Phosphide of zinc, 121.
Phosphoric acid, 453.
Phosphorus, 112.
  antidote to, 119.
Physostigma, 342.
Physostigmine, 342.
Picra-aconitine, 186.
Picric acid, 86.
Pikropodophyllin, 514.
Pill of aloes, 507.
  of aloes and assafetida, 507.
  of aloes and mastic, 507.
  of aloes and myrrh, 507.
  of assafetida, 215.
  of carbonate of iron, 101.
  of iron, 101.
  of mercury, 432.
  of opium, 254.
  of rhubarb, 504.
Pilocarpine, 559, 565.
  antagonism with atropia, 565.
Pilula ferri carbonatis, 101.
Pilulæ, 19.
  assafœtidæ, 215.
  catharticæ compositæ, 514.
  ferri compositæ, 101.
  phosphori, 121.
  rhei, 504.
  rhei compositæ, 504.
Pimenta, 90.
Pimento, 90.
Pinkroot, 648.
Piper, 91.
Piperin, 91.
Pipsissewa, 545.
Pitch, 582.
Pix Burgundica, 618.
  Canadensis, 618.
  liquida, 582.
Plasma, 635.
Plaster of ammoniac, with mercury, 577.
  of Burgundy pitch, 618.
  of Canada pitch, 618.
  of pitch with cantharides, 618.
Plumbi acetas, 42.
  carbonas, 43.
  nitras, 43.
  oxidum, 42.
Plumbum, 34.
Podophyllin, 514.
Podophyllinic acid, 514.
Podophyllotoxin, 514.
Podophyllum, 514.
Polygalic acid, 576.
Pomegranate rind, 654.
Poppy, 240.
Porphyroxia, 262.
Potassa, 620.
  cum calce, 621.
  sulphurata, 497.
Potassii acetas, 534.
Potassii bicarbonas, 534.
  bitartras, 536.
  bromidum, 356.
  carbonas, 534.
  chloras, 539.
  citras, 534.
  cyanidum, 206.
  et sodii tartras, 510.
  iodidum, 442.
  nitras, 536.
  nitris, 389.
  permanganas, 669.
  sulphas, 510, 536.
  tartras, 536.
Potassium, 528.
Potentilla tormentilla, 32.
Poultices, 635.
Precipitated carbonate of calcium, 455, 646.
  carbonate of iron, 100.
  carbonate of zinc, 45.
  phosphate of calcium, 454.
  sulphur, 496.
Prepared chalk, 346.
  oyster-shell, 346.
Prescribing, art of, 743.
Pride of China, 649.
Primary current, 743.
Propenyl alcohol, 632.
Propylamin, 590.
Protectives, 638.
Protiodide of mercury, 436.
Prunes, 494.
Prunus Virginiana, 62.
Prussic acid, 196.
Pseudaconitia, 185.
Pseudomorphia, 263.
Puccin, 476.
Pulveres, 19.
  aromaticus, 89.
  effervescentes compositus, 510.
  glycyrrhizæ compositus, 508.
  ipecacuanhæ et opii, 558.
  jalapæ compositus, 512.
  rhei compositus, 504.
Pulvis parturiens, 598
Pumpkin seed, 654.
Purgative enemas, 490.
Purgatives, 483.
Purges, 498.
Purging cassia, 495.
Purified aloes, 507.
  animal charcoal, 661.
  chloroform, 316.
Pyrethrum, 605.
Pyrogallic acid, 27.
Pyrophosphate of iron, 104.
Pyroxylin, 638.
Pyroxylum, 638.

Q.

Quassia, 59.
Quassin, 59.
Quercitron, 31.

- Quercus alba, 31.
  - tinctoria, 31.
- Quevenne's iron, 100.
- Quince seed, 628.
- Quinidine, 84.
- Quinidinæ sulphas, 84.
- Quinina, 64.
  - as an abortifacient, 74.
  - as an antipyretic, 78.
  - bromide of, 84.
  - dihydroxyle, 77.
  - tannate of, 84.
- Quininæ sulphas, 64.
- Quinoidin, 86.
- Quinoidine (animal), 80.

R.

- Reactions of degeneration, 732.
- Red cinchona, 64.
  - ipecacuanha, 471.
  - iodide of mercury, 436.
  - oxide of mercury, 436.
  - precipitate, 436.
  - rose, 31.
  - sulphuret of mercury, 436.
  - wine, 126.
- Reduced iron, 100.
- Refrigerant diaphoretics, 559.
- Refrigerants, 207.
- Rennet, 656.
- Resin of jalap, 512.
  - of May-apple, 575.
  - of podophyllum, 575.
  - of scammony, 514.
  - of veratrum viride, 514.
  - of plaster, 42, 140.
- Resina, 140.
- Resinæ, 18.
- Rhabarbin, 503.
- Rhamnus, 495.
- Rhatany, 31.
- Rhein, 503.
- Rheum, 502.
- Rhodeoretin, 511.
- Rhubarb, 502.
- Rhus glabra, 32.
- Rochelle salt, 510.
- Roman chamomile, 89.
- Rosa centifolia, 32.
  - Gallica, 31.
- Rosemary, 93.
- Rose-water, 32.
- Rosin, 140.
- Rosmarinus, 93.
- Rottlera, 655.
- Rottlerin, 655.
- Royal yellow bark, 64.
- Rubefacients, 609, 615.
- Rubus, 32.
- Rue, 586.
- Russian bath, 553.
- Ruta, 586.
- Rutin, 586.

S.

- Sabadilla, 178.
- Sabadilline, 178.
- Sabina, 585.
- Saccharate of lime, 687.
- Saccharated carbonate of iron, 101.
  - iodide of iron, 103.
- Saccharum, 493.
- Saccharum lactis, 493.
- Sage, 93.
- Sago, 629.
- Sal ammoniac, 574.
  - prunelle, 537.
- Salicin, 699.
- Salicylic acid, 689.
  - as an antipyretic, 696.
  - wadding, 697.
- Salicyluric acid, 694.
- Saline cathartics, 485.
  - purgatives, 485, 508.
- Salseparin, 463.
- Salt of lemons, 211.
- Salt of sorrel, 211.
- Saltpetre, 536.
- Salvia, 93.
- Sanguinaria, 476.
- Sanguinarine, 476.
- Santoninate of sodium, 654.
- Santonica, 650.
- Santonin, 650.
- Santoninic acid, 650.
- Santonicum, 650.
- Saponin, 576.
- Sarsaparilla, 463.
- Sarsaparillin, 463.
- Sassafras, 468.
  - pith, 628.
- Savine, 585.
- Scammonium, 513.
- Scammony, 513.
- Scilla, 521.
- Scillaine, 521.
- Scilline, 521.
- Scillipicrine, 521.
- Scillitine, 521.
- Scillitoxine, 521.
- Sclerotinic acid, 590.
- Sclerotium, 589.
- Scoparine, 527.
- Scoparius, 527.
- Scudamore's mixture, 461.
- Sculein, 521.
- Seidlitz powders, 510.
- Senega, 576.
- Seneka, 576.
- Senna, 507.
- Septfoil, 32.
- Serpentaria, 89.
- Sesquichloride of iron, 102.
- Shore oil, 448.
- Sialagogues, 605.
- Silver, 49.
- Simaruba, 59.
- Simple bitters, 58.
- Sinapin, 616.
- Sinapinic acid, 616.
- Sinapis alba, 615.
  - nigra, 615.
- Sinapisin, 616.
- Sipeeria, 60.
- Slippery elm bark, 626.
- Smelling-salts, 606.
- Smilacin, 463.
- Smut of Indian corn, 604.
- Soap liniment, 218.
  - plaster, 42, 638.
- Socotrine aloes, 505.
- Soda, 644.
  - powders, 644.
- Sodii acetas, 645.
  - arsenias, 423.
  - biboras, 673.
  - bicarbonas, 644.
  - bicarbonas venalis, 644.
  - bromidum, 366.
  - carbonas, 644.
  - carbonas exsiccata, 644.
  - nitras, 645.
  - phosphas, 510.
  - sulphas, 509.
- Sodium, 642.
- Solution of acetate of ammonium, 566.
  - of arseniate of sodium, 423.
  - of arsenious acid, 423.
  - of arsenite of potassium, 423.
  - of chloride of zinc, 623.
  - of chlorinated soda, 673.
  - of citrate of magnesium, 509.
  - of citrate of potassium, 534.
  - of gutta-percha, 640.
  - of iodide of arsenic and mercury, 444.
  - of lime, 645.
  - of nitrate of mercury, 623.
  - of permanganate of potassium, 671.
  - of persulphate of iron, 102.
  - of potassa, 642.
  - of soda, 644.
  - of subacetate of lead, 43.
  - of subsulphate of iron, 102.
  - of sulphate of morphia, 255.
  - of tersulphate of iron, 102.
- Spanish flies, 611.
- Spartein, 527.
- Spasmodic ergotism, 603.
- Spearmint, 93.
  - water, 93.
- Spermaceti, 631.
- Spice plasters, 617.
- Spigelia, 648.
- Spinal cord, galvanization of, 736.
- Spirit of ammonia, 126.
  - of anise, 93.
  - of camphor, 218.
  - of chloroform, 324.
  - of cinnamon, 91.

- Spirit of juniper, 546.
  - of lavender, 93.
  - of lemons, 93.
  - of Mindererus, 566.
  - of nitrous ether, 528, 566.
  - of peppermint, 93.
  - of spearmint, 93.
- Spiritus, 18.
  - ætheris compositus, 220.
  - ætheris nitrosi, 566.
  - ammoniæ, 126.
  - ammoniæ aromaticus, 126.
  - chloroformi, 324.
  - frumenti, 126.
  - vini Gallici, 126.
- Squill, 521.
  - as an emetic, 482.
  - as an expectorant, 582.
- St. Ignatius' bean, 341.
- Star anise, 93.
- Sticking plaster, 42, 140.
- Stigmata of Zea mays, 546.
- Stimulating diuretics, 546.
- Stomach pump siphon, 252.
- Straits oil, 448.
- Stramonii folia, 296.
  - semen, 296.
- Stramonium leaves, 296.
  - seed, 296.
- Stronger alcohol, 126.
  - ether, 387.
  - water of ammonia, 126.
- Strychninæ sulphas, 341.
- Strychnine, 326.
  - poisoning by, 336.
- Subacetate of copper, 49.
  - of lead, 43.
- Subcarbonate of bismuth, 44.
  - of iron, 100.
- Sublimed sulphur, 496.
- Subnitrate of bismuth, 44.
- Succi, 18.
- Succinum, 220.
- Succus conii, 406.
  - limonis, 209.
- Sugar, 494.
  - of lead, 42.
  - of milk, 493.
- Sulphate of aluminium, 34.
  - of ammonium, 126, 574.
  - of atropine, 290.
  - of bebeerine, 60.
  - of cadmium, 47.
  - of cinchonidine, 84.
  - of cinchonine, 84.
  - of copper, 482, 624.
  - of hyoscyamine, 277.
  - of iron, 101.
  - of iron and ammonium, 104.
  - of manganese, 104.
  - of magnesium, 508.
  - of morphia, 255.
  - of potash, 510, 536.
  - of quinidine, 84.
  - of quinine, 64.
  - of sodium, 510.
  - of strychnine, 341.
- Sulphate of zinc, 46, 482, 624.
- Sulphide of calcium, 498.
- Sulphites, 675.
- Sulpho-sinapisin, 616.
- Sulphovinate of sodium, 511.
- Sulphur, 496.
  - lotum, 496.
  - ointment, 497.
  - præcipitatum, 496.
  - sublimatum, 496.
- Sulphurated antimony, 163.
  - lime, 498.
  - potassa, 497.
- Sulphuret of antimony, 163.
  - of potassa, 497.
- Sulphuric acid, 105.
  - as a caustic, 623.
- Sulphurous acid, 675.
- Sumach, 542.
- Suppositoria, 19.
- Suppositories of assafetida, 215.
  - of lead, 43.
  - of morphia, 256.
  - of tannic acid, 29.
- Sweet orange peel, 93.
- Sweet spirit of nitre, 528, 566.
- Sydenham's laudanum, 255.
- Sympathetic, galvanisation of, 738.
- Syrup, 18.
  - of acacia, 625.
  - of althæa, 628.
  - of ginger, 91.
  - of iodide of iron, 103.
  - of ipecacuanha, 475.
  - of krameria, 31.
  - of lime, 646.
  - of red rose, 32.
  - of rhatany, 31.
  - of rhubarb, 504.
  - of sarsaparilla, compound, 464.
  - of seneka, 577.
  - of senna, 508.
  - of squill, 525, 582.
  - of sweet orange peel, 93.
  - of the phosphates, compound, 456.
  - of tar, 583.
  - of Tolu, 581.
  - of wild cherry, 63.
- Syrupi, 18.
- Syrupus calcis, 646.
  - fuscus, 493.

T.

- Tabacum, 396.
- Table of proportion by measure of alcohol contained in one hundred parts of different wines, etc., 749.
- Table of relation of weights and measures of the U. S. Pharmacopœia to each other, 747.
- Tables of relation of weights of the U.S.Pharmacopœia to metrical weights, 749.
- Table of weights and measures of the metrical system, 747.
- Table of weights and measures of the U. S. Pharmacopœia, 748.
- Table showing results of cold-water treatment of typhus and typhoid fever, 711.
- Tæniin, 650.
- Tamarind, 494.
- Tamarindus, 494.
- Tanacetum, 586.
- Tannate of quinine, 84.
  - of cannabene, 268.
- Tannic acid, 26.
- Tansy, 586.
- Tapioca, 628.
- Tar, 582.
  - ointment, 583.
  - water, 583.
- Taraxacum, 468.
- Tartar, 207.
- Tartar emetic, 163, 482, 573.
  - antidote to, 28.
- Tartaric acid, 207.
- Tartrate of antimony and potassium, 163.
  - of iron and ammonium, 104.
  - of iron and potassium, 104.
  - of potassium, 536.
  - of potassium and sodium, 510.
- Temperament, 22.
- Terchloride of formyl, 315.
- Terebinthina, 140, 546.
  - Canadensis, 546.
- Tersulphuret of antimony, 163.
- Thebaia, 260.
- Theine, 223.
- Therapeutics, 17.
- Thymol, 699.
- Tinctura ferri chloridi, 102.
  - opii, 255.
  - opii acetata, 255.
  - opii camphorata, 254.
  - opii deodorata, 255.
- Tincturæ, 18.
- Tincture of aconite, 195.
  - of aloes, 150.
  - of aloes and myrrh, 150.
  - of arnica, 578.
  - of assafetida, 215.
  - of belladonna, 270.
  - of benzoin, 581.
  - of bitter orange peel, 93.
  - of black hellebore, 520.
  - of bloodroot, 477.
  - of Calabar bean, 353.
  - of cantharides, 552, 614.
  - of capsicum, 91.
  - of cardamom, 90.

Tincture of castor, 213.
  of catechu, 30.
  of chiretta, 62.
  of chloride of iron, 102.
  of cimicifuga, 223.
  of cinchona, 86.
  of cinnamon, 89.
  of colchicum, 462.
  of columbo, 61.
  of conium, 406.
  of cubeb, 552.
  of digitalis, 158.
  of eucalyptus, 97.
  of galls, 30.
  of gelsemium, 396.
  of gentian, 60.
  of ginger, 91.
  of guaiac, 467.
  of guaiac, ammoniated, 467.
  of hellebore, 520.
  of hemp, 268.
  of hops, 221.
  of hyoscyamus, 299.
  of ignatia, 341.
  of iodine, 442.
  of kino, 30.
  of lobelia, 392.
  of lupulin, 221.
  of matico, 552.
  of musk, 213.
  of nutgall, 30.
  of nux vomica, 326.
  of opium, 255.
  of opium, acetated, 255.
  of opium, camphorated, 254.
  of opium, deodorized, 255.
  of quassia, 59.
  of rhubarb, 504.
  of rhubarb and senna, 504.
  of sanguinaria, 477.
  of serpentaria, 89.
  of squill, 525.
  of stramonium, 297.
  of sweet orange peel, 93.
  of Tolu, 581.
  of valerian, 214.
  of valerian, ammoniated, 214.
  of veratrum viride, 176.
Tobacco, 396.
Tonics, 58.
Tormentil, 32.
Tormentilla, 32.
Tous des mois, 630.
Toxiresin, 144.
Tragacanth, 626.
Tragacantha, 626.
Trimethylamin, 449, 590.
Trinitro-cellulose, 638.
Tripoli senna, 507.
Trituration of elaterium, 517.
Troches, 19.
Trochisci ipecacuanhæ, 476.
  morphinæ et ipecacuanhæ, 476.
  ammonii chloridi, 576.
Trypsin, 658.
Turkish bath, 553.
Turpentine, 140, 546, 654.
  stupes, 142, 617.
Turpeth mineral, 436.

U.

Ulmus, 626.
  fulva, 626.
Unguenta, 19.
Unguentum antimonii, 169.
  aquæ rosæ, 32, 632.
  hydrargyri, 432.
  hydrargyrum ammoniatum, 437.
  mezereon, 465.
  picis liquidæ, 583.
  plumbi carbonati, 43.
  potassii iodidi, 444.
  veratrinæ, 184.
  zinci oxidi, 46.
Urea, elimination of, by the skin, 557.
Urochloralic acid, 372.
Urobutylchloralic acid, 380.
Ursin, 544.
Urson, 544.
Ustilago maidis, 604.
Uva ursi, 544.

V.

Valerian, 213.
Valeriana, 213.
Valerianate of ammonium, 214.
  of amyl, 391.
Valerianic acid, 214.
Vapor bath, 553.
Vegetable acids, 206.
Veratralbia, 176.
Veratrine, 176, 178.
  ointment, 184.
Veratroidia, 170.
Veratrum album, 176.
  viride, 169, 559.
  viride as a diaphoretic, 559.
  viride, resin of, 170.
  viride, tincture of, 170.
Verdigris, 49.
Vermicides, 648.
Vermifuges, 648.
Vienna paste, 622.
Vina, 18.
Vinegar, 210.
  of bloodroot, 477.
  of lobelia, 392.
  of opium, 255.
  of sanguinaria, 477.
  of squill, 525.
Vinum album, 126.
  rubrum, 126.
Virginia snakeroot, 89.
Viridia, 170.
Vitriolated tartar, 510.
Vomiting, 468, 470.
Vomiting, treatment of excessive, 470.

W.

Wahoo, 508.
Warburg's tincture, 568.
Warming plaster, 618.
Washed sulphur, 496.
Water of ammonia, 126, 611.
Wax water, 632.
  as a diuretic, 521.
Weights and measures of the metrical system, 7.
Weights and measures of the United States Pharmacopœia, 7.
West India pepper, 92.
Wheat, cracked, 493.
Whisky, 126.
White arsenic, 409.
  galls, 30.
  ginger, 91.
  hellebore, 176.
  lead, 43.
  mustard, 616.
  oak, 31.
  pepper, 91.
  precipitate, 437.
  precipitate ointment, 437.
  sugar, 464.
  turpentine, 140.
  vitriol, 45.
  wax, 632.
  wine, 126.
Wild cherry, 62.
Wine of aloes, 507.
  of antimony, 169.
  of colchicum root, 462.
  of colchicum seed, 462.
  of ergot, 603.
  of ipecacuanha, 475.
  of lobelia, 392.
  of opium, 255.
  of rhubarb, 504.
  whey, 139.
Wormseed, 649.
  oil, 649.

Y.

Yaupon, 223.
Yeast, 656.
Yellow cinchona, 64.
  jessamine, 392.
  oxide of mercury, 436.
  sulphate of mercury, 436.
  wash, 436.
  wax, 632.
Young's rule for doses, 22.

Z.

Zea mays, stigmata of, 546.
Zinc, 45.
  phosphide of, 121.
Zinci acetas, 46.
  carbonas præcipitata, 46.
  chloridum, 622.
  oxidum, 46.
  oxidum venale, 46.
  sulphas, 45.
Zincum, 45.
Zingiber, 91.

INDEX OF DISEASES.

A.

- *Abscess:*
  - tannic acid, 28.
  - alcohol, 137.
  - carbolic acid, 680.
  - permanganate of potassium, 670.
- *Acidity of stomach:*
  - ammonia, 125.
- *Acne:*
  - arsenic, 419.
  - iodine, 441.
  - phosphorus, 113.
  - solution of nitrate of mercury, 623.
- *Acne rosacea:*
  - cajeput, 92.
  - solution of nitrate of mercury, 623.
- *Aconite-poisoning:*
  - alcohol, 137.
  - treatment, 194.
- *Adynamic fevers:*
  - ammonia, 124.
  - alcohol, 136.
  - camphor, 218.
  - digitalis, 156.
  - mineral acids, 107.
  - opium, 251.
  - chlorate of potassium, 541.
  - acetate of ammonium, 566.
  - spirit of nitrous ether, 567.
  - turpentine, 142.
  - valerian, 214.
- *Alcoholic intoxication:*
  - ammonia, 125.
- *Alimentary inflammation:*
  - demulcents, 625.
- *Alopecia:*
  - jaborandi, 564.
- *Amaurosis:*
  - strychnine, 335.
  - santonin, 653.
- *Amenorrhœa:*
  - carbonate of iron, 101.
  - cantharides, 587.
  - aloes, 506.
  - turpentine, 547.
  - alcohol, 567.
  - seneka, 577.
- *Amenorrhœa:*
  - emmenagogues, 584.
  - myrrh, 584.
  - hellebore, 585.
  - iron, 585.
  - savine, 586.
  - rue, 586.
  - apiol, 587.
  - guaiac, 588.
  - cotton root, 604.
- *Anæmia:*
  - iron, 97, 100.
- *Anæsthesia of skin:*
  - electricity, 735.
- *Aneurism:*
  - digitalis, 155.
  - iodide of potassium, 443.
  - ergot, 600.
- *Angina:*
  - gum arabic, 625.
- *Angina pectoris:*
  - nitrite of amyl, 387.
  - nitrite of potassium, 389.
  - nitrite of sodium, 390.
  - nitroglycerine, 390.
  - chlorate of potassium, 541.
- *Animal poisoning:*
  - ammonia, 125.
  - alcohol, 137.
- *Aortic disease:*
  - digitalis, 154.
- *Aphthous sore mouth:*
  - chlorate of potassium, 541.
  - borax, 675.
  - carbolic acid, 683.
- *Arsenical poisoning:*
  - treatment, 422.
- *Arterial excitement:*
  - aconite, 193.
  - antimony, 167.
  - gelsemium, 395.
  - veratrum viride, 174.
- *Ascites:*
  - elaterium, 517.
  - chlorate of potassium, 541.
  - jalap, 512.
- *Asthma:*
  - eucalyptus, 97.
  - belladonna, 287.
- *Asthma:*
  - emetics, 469.
  - gelsemium, 395.
  - hyoscine, 300.
  - stramonium, 297.
  - anæsthetics, 305.
  - ether, 315.
  - chloral, 375.
  - nitrite of amyl, 387.
  - lobelia, 392.
  - nitroglycerine, 391.
  - tobacco, 400.
  - arsenic, 420.
  - iodide of potassium, 443.
- *Atheroma:*
  - digitalis, 155.

B.

- *Bed-sores:*
  - chloral, 376.
  - protectives, 638.
- *Belladonna-poisoning:*
  - treatment, 294.
- *Biliary calculi:*
  - belladonna, 287.
  - emetics, 469.
- *Bilious fever:*
  - quinia, 82.
  - calomel, 502.
  - jaborandi, 564.
  - Warburg's tincture, 568.
- *Biliousness:*
  - muriate of ammonia, 576.
  - nitro-muriatic acid, 110.
  - calomel, 502.
  - podophyllum, 515.
  - potassium salts, 535.
- *Bites:*
  - caustic potash, 620.
- *Bladder, irritable:*
  - buchu, 543.
  - hops, 221.
  - pareira, 544.
  - Indian corn silk, 546.
- *Boils:*
  - cocaine, 238.
  - phosphorus, 113.
  - sulphide of calcium, 498.

Boils:
  sulphurated lime, 498.
Brain softening:
  phosphorus, 113.
Bright's disease:
  caffein, 231.
  cream of tartar, 536.
  jaborandi, 564.
  gallic acid, 29.
  iodide of potassium, 443.
  tincture of the chloride of iron, 102.
  diuretics, 521.
  diaphoretics, 556.
  water, 521, 635.
Bronchitis:
  antimony, 168.
  apomorphia, 481.
  assafetida, 215.
  Calabar bean, 352.
  benzoic acid, 581.
  oil of amber, 220.
  lobelia, 392.
  oil of eucalyptus, 97.
  oil of turpentine, 142, 143.
  tartar emetic, 572.
  cimicifuga, 223.
  opium, 250.
  lobelia, 392.
  sanguinaria, 477.
  copaiba, 550.
  cubebs, 551.
  expectorants, 569.
  inhalations, 572.
  ipecacuanha, 572.
  chloral, 375.
  chloride of ammonium, 575.
  seneka, 576.
  alkalies, 569.
  ammoniac, 577.
  garlic, 582.
  squill, 582.
  strychnine, 335.
  tar, 583.
  Burgundy pitch, 618.
  demulcents, 625.
  liquorice, 628.
Bronchorrhœa:
  gallic acid, 29, 569.
  alum, 33.
  astringents, 571.
Buboes:
  iodoform, 447.
  chloral, 376.
Burns:
  Carron oil, 646.
  carbonate of lead, 43.
  carbolic acid, 685.
  Kentish ointment, 618.
  chalk, 647.
Bursæ, inflamed:
  carbolic acid injections, 684.

C.

Cachexia:
  glycerine, 634.
Calculi:
  anæsthetics, 305.
  benzoic acid, 580.
Cancer:
  arsenic, 621.
  Chian turpentine, 143.
  chloral, 376.
  conium, 406.
  acid nitrate of mercury, 623.
  iodoform, 447.
Cancrum oris:
  nitric acid, 108.
Carcinoma of stomach:
  bismuth, 45.
Cardiac disease, chronic:
  aconite, 193.
  digitalis, 152.
  Hoffmann's anodyne, 220.
  nitrite of amyl, 387.
  veratrum viride, 175.
Cardiac dropsy:
  caffein, 231.
  squill, 525.
  digitalis, 159.
Cardiac failure:
  ammonia, 125.
  nitrite of amyl, 387.
Cardialgia:
  antacids, 641.
  charcoal, 662.
Caries:
  cod-liver oil, 451.
  cloves, 90.
Cataract:
  phosphorus, 113.
  atropia, 292.
Catarrh:
  balsam of Peru, 581.
  chloride of ammonium, 576.
Catarrh, chronic:
  assafetida, 215.
  benzoic acid, 580.
  expectorants, 569.
Catarrh of bladder:
  benzoic acid, 581.
  juniper, 545.
  thymol, 700.
Catarrh, suffocative:
  allium, 582.
  apomorphia, 480.
  expectorants, 569.
Catarrhal pneumonia:
  cod-liver oil, 451.
  alteratives, 569.
Cerebral excitement:
  bromide of potassium, 362.
Cerebritis:
  electricity, 736.
Chancres:
  iodoform, 447.
  escharotics, 619.
  Canquoin's paste, 622.
  solution of nitrate of mercury, 623.
  corrosive sublimate, 623.
Chancres:
  black and yellow washes, 437.
  chloride of zinc, 622.
  nitric acid, 108.
Chapped hands, lips, nipples:
  benzoic acid, 581.
  solution of gutta-percha, 640.
Chloral poisoning:
  treatment of, 377.
Cholera:
  ammonia, 125.
  camphor, 216.
  chloral, 375.
  sulphuric acid, 105.
  nitrite of amyl, 388.
Cholera infantum:
  sulphuric acid, 105.
  chlorate of potassium, 541.
  cold, 716.
Chordee:
  brominated camphor, 219.
  hops, 221.
  camphor, 218.
Chorea:
  arsenic, 420.
  Calabar bean, 342.
  cimicifuga, 221.
  chloral, 375.
  conium, 406.
  bromide of iron, 104.
  bromide of sodium, 366.
  lobelia, 392.
  oxide of zinc, 46.
Cirrhosis:
  nitro-muriatic acid, 110.
Cold, a general:
  Dover's powder, 558.
  hot baths, 556.
Colic:
  assafetida, 215.
  atropia, 287.
  belladonna, 287.
  cajeput, 92.
  chloroform, 322.
  ether, 315.
  antacids, 641.
  ginger, 91.
  opium, 250.
Colica pictonum:
  alum, 33.
  sulphuric acid, 107.
  belladonna, 287.
  chloroform, 322.
  Epsom salt, 509.
Colitis:
  nitrate of silver, 55.
  sulphate of magnesium, 509.
Collapse:
  ammonia, 125.
  digitalis, 155.
  heat, 704.
  mustard, 609.

- *Collapse :*
  - Warburg's tincture, 568.
- *Colliquative sweats :*
  - gallic acid, 29.
  - alum, 33.
  - sulphuric acid, 105.
  - belladonna, 288.
  - ergot, 599.
  - ipecacuanha, 474.
- *Condylomata :*
  - nitric acid, 623.
  - chromic acid, 624.
  - carbolic acid, 683.
- *Congestion of brain :*
  - elaterium, 517.
- *Congestion of cord :*
  - ergot, 600.
- *Congestion, hepatic :*
  - nitro-muriatic acid, 110.
- *Congestion, renal :*
  - juniper, 545.
- *Conjunctivitis :*
  - alum, 33.
  - sulphate of copper, 47.
  - nitrate of silver, 53.
  - yellow oxide of mercury, 436.
- *Constipation :*
  - alum, 34.
  - aloes, 506.
  - belladonna, 287.
  - Epsom salts, 509.
  - strychnine, 336.
  - general treatment, 491.
  - Calabar bean, 353.
  - cascara sagrada, 495.
  - castor oil, 499.
  - podophyllum, 515.
  - cracked wheat, 494.
  - bran, 494.
  - unbolted flour, 494.
  - Indian meal, 494.
  - forced enemata, 490.
  - rhubarb, 504.
  - gamboge, 519.
  - croton oil, 520.
  - wahoo, 508.
- *Consumption :*
  - cod-liver oil, 451.
- *Convulsions :*
  - anæsthetics, 305.
  - bromide of potassium, 362.
  - brominated camphor, 219.
  - chloral, 375.
  - emetics, 469.
  - garlic, 582.
  - lobelia, 392.
  - nitrite of amyl, 388.
- *Coryza :*
  - cocaine, 238.
  - cubebs, 606.
  - errhines, 606.
  - glycerine, 737.
  - nitrite of amyl, 388.
- *Cough, to quiet :*
  - belladonna, 287.
  - prussic acid, 204.
- *Cramps of pregnancy :*
  - chloral, 375.
- *Croup, membranous :*
  - alum, 33, 482.
  - glycerine, 737.
  - ipecacuanha, 474.
  - jaborandi, 565.
  - lime-water, 646.
  - mercury, 429.
- *Cystitis, chronic :*
  - arbutin, 544.
  - boracic acid, 675.
  - buchu, 543.
  - iodine, 441.
  - pareira, 543.
  - uva ursi, 544.
  - turpentine, 547.
  - copaiba, 549.
  - cantharides, 552.
  - salicylic acid, 697.
  - zea mays, 546.
- *Cystorrhœa :*
  - ergot, 601.

D.

- *Debility :*
  - prunus Virginiana, 63.
- *Delirium of low fevers :*
  - musk, 213.
  - valerian, 214.
  - opium, 250.
  - chloral, 375.
  - blisters, 610.
- *Delirium tremens :*
  - brominated camphor, 219.
  - veratrum viride, 174.
  - hops, 221.
  - opium, 250.
  - bromide of potassium, 362.
  - chloral, 373.
  - croton oil, 519.
  - gamboge, 520.
- *Dermal growths :*
  - chromic acid, 623.
  - nitric acid, 624.
- *Diabetes :*
  - opium, 250.
  - glycerine, 737.
  - thymol, 700.
  - yeast, 650.
- *Diabetes insipidus :*
  - opium, 250.
- *Diarrhœa :*
  - aromatics, 88.
  - tannic acid, 28.
  - catechu, 30.
  - coca, 238.
  - antacids, 641.
  - hæmatoxylon, 31.
  - alum, 33.
  - acetate of lead, 42.
  - bismuth, 45.
  - eucalyptus, 97.
  - oil of cajeput, 92.
  - ipecacuanha, 474.
  - sulphuric acid, 106.
  - magnesia, 496.
  - nitrous acid, 109.
  - camphor, 216.
  - opium, 250.
  - pepsin, 658.
  - belladonna, 288.
  - strychnine, 330.
  - castor oil, 499.
  - rhubarb, 504.
  - ergot, 600.
  - lime-water, 646.
  - charcoal, 662.
- *Diarrhœa, chronic :*
  - bismuth, 45.
  - sulphate of copper, 47.
  - sulphate of iron, 102.
  - sulphate of zinc, 46.
  - nitro-muriatic acid, 110.
  - magnesia, 496.
  - oxide of zinc, 46.
  - copaiba, 549.
  - ergot, 600.
  - phosphate of sodium, 510.
- *Dilatation of heart :*
  - digitalis, 152.
  - convallaria, 160.
- *Diphtheria :*
  - benzoic acid, 580.
  - carbolic acid, 685.
  - cold, 706.
  - borax, 675.
  - jaborandi, 564.
  - tincture of the chloride of iron, 162.
  - muriatic acid, 107.
  - chlorate of potassium, 541.
  - lime-water, 656.
  - salicylic acid, 696.
- *Diphtheritic paralysis :*
  - electricity, 731.
- *Dislocation :*
  - anæsthetics, 305.
- *Diuresis, excessive :*
  - turpentine, 547.
- *Dropsy :*
  - antihydropin, 542.
  - bitartrate of potassium, 536.
  - caffein, 231.
  - colocynth, 513.
  - convallarin, 160.
  - copaiba, 550.
  - digitalis, 160, 525.
  - elaterium, 517.
  - gamboge, 518.
  - hot baths, 556.
  - jaborandi, 564.
  - jalap, 512.
  - scoparius, 528.
  - senega, 577.
  - squill, 525.
  - veratria, 184.
- *Dysentery :*
  - acetate of lead, 42.

Dysentery:
cathartics, 492.
cold, 717.
nitrous acid, 109.
opium, 250, 254.
iodine, 441.
ipecacuanha, 474.
calomel, 502.
castor oil, 499.
chlorate of potassium, 541.
copaiba, 549.
ergot, 600.
flaxseed, 628.
glycerine, 737.
Dysmenorrhœa:
acetate of ammonium, 566.
aloes, 506.
apiol, 587.
ginger, 91.
belladonna, 218.
camphor, 218.
guaiac, 587.
nitrite of amyl, 388.
cotton root, 604.
Dyspepsia:
alcohol, 138.
charcoal, 662.
ginger, 91.
piperin, 92.
magnesia, 496.
pepsin, 657.
muriatic acid, 107.
nitrate of silver, 54.
pepper, 92.
nitric acid, 108.
assafetida, 215.
strychnine, 336.
Calabar bean, 353.
antacids, 641.
taraxacum, 466.
wahoo, 508.
Dysuria:
conium, 406.

E.

Eczema:
arsenic, 419.
glycerine, 737.
oxide of zinc ointment, 46.
Effusion, pericardial:
squill, 525.
Effusion, pleural:
squill, 525.
Emphysema:
strychnine, 336.
Empyema:
iodine, 442.
Endocarditis:
mercury, 429.
Enteritis:
nitrate of silver, 55.
opium, 250.
sulphate of magnesium, 509.
Enteritis:
chlorine, 671.
castor oil, 499.
flaxseed, 628.
slippery elm, 626.
Enteritis, obstructive:
calomel, 502.
ulmus fulva, 626.
flaxseed, 628.
Epididymitis:
nitrate of silver, 54.
Epilepsy:
oxide of zinc, 46.
ammoniated copper, 48.
nitrate of silver, 55.
camphor, 218.
bromide of camphor, 219.
ergot, 600.
anæsthetics, 305.
Calabar bean, 353.
bromide of potassium, 362.
bromide of sodium, 366.
bromide of lithium, 366.
bromide of ammonium, 365.
lobelia, 392.
nitrite of amyl, 388.
santonin, 653.
Epistaxis:
tannic acid, 28.
ergot, 599.
Erysipelas:
nitrate of silver, 54.
benzoic acid, 580.
borax, 674.
sulphate of iron, 101.
tincture of the chloride of iron, 102.
belladonna, 288.
quinia, 79.
iodine, 441.
carbolic acid injections, 685.
Exophthalmic goitre:
iodine, 441.

F.

Failure of heart:
ammonia, 125.
digitalis, 155.
Fatty heart:
nitrite of amyl, 388.
Faucitis:
nitrate of silver, 53.
Fecal accumulation:
black draught, 508.
Epsom salt, 509.
Feet, tender:
tannic acid, 28.
Felon:
nitrate of silver, 54.
carbolic acid, 684.
Fetid expectoration:
carbolic acid, 572.
Fever:
antipyrin, 701.
kairin, 703.
digitalis, 156.
aconite, 193.
cold, 707.
chloral, 373.
gelsemium, 395.
muriatic acid, 107.
nitric acid, 108.
ammonia, 125.
tartar emetic, 168.
lemon-juice, 209.
Fibroid tumors of uterus:
ergotin, 600.
Fissure of anus:
belladonna, 287.
benzoic acid, 581.
Fragilitas ossium:
phosphates, 454.
Furuncles:
See Boils.

G.

Galactorrhœa:
ergot, 600.
Gangrene:
nitric acid, 108.
carbolic acid, 683.
Gangrene, hospital:
bromine, 624.
nitric acid, 108.
Gastralgia:
alum, 34.
bismuth, 45.
manganese, 105.
prussic acid, 204.
arsenic, 420.
Gastric catarrh:
chloride of ammonium, 576.
bismuth, 45.
Gastric ulcer:
nitrate of silver, 55.
oil of turpentine, 142.
Gastritis:
nitrate of silver, 55.
veratrum viride, 174.
Glands, enlarged:
ammoniac, 577.
carbolic acid injections, 684.
conium, 406.
iodine, 442.
mercury, 432.
sulphurated lime, 498.
cod-liver oil, 145.
Glaucoma:
atropia, 293.
Gleet:
tincture of the chloride of iron, 102.
turpentine, 547.
cantharides, 552.
Goitre:
iodine, 441.
Gonorrhœa:
acetate of zinc, 47.
antimony, 167.

Gonorrhœa:
arbutin, 544.
benzoic acid, 580.
bismuth, 45.
bromide of potassium, 363.
eucalyptus, 97.
nitrate of silver, 53, 54.
oil of erigeron, 546.
tartar emetic, 167.
pareira, 543.
copaiba, 549.
cubebs, 551.
matico, 552.
quinia, 83.
water, 637.
Gonorrhœal rheumatism:
salicylic acid, 696.
Gout:
arsenic, 420.
carbonate of lithium, 542.
ether, 315.
iodide of potassium, 452.
lithium, 542.
magnesia, 496.
cod-liver oil, 452.
colchicum, 460.
potassium, 532.
rubefacients, 615.
Gout, retrocedent:
ether, 315.
Granulations, exuberant:
burnt alum, 624.
sulphate of copper, 624.
sulphate of zinc, 624.
Gravel:
stigmata of Indian corn, 546.
water, 637.
benzoic acid, 580.
Graves's disease:
iodine, 441.
Gums, retraction of:
iodine, 441.

H.

Hæmatemesis:
tannic acid, 28.
gallic acid, 29.
subsulphate of iron, 102.
oil of turpentine, 143.
Hæmaturia:
gallic acid, 29.
turpentine, 547.
Hæmoptysis:
alum, 33.
acetate of lead, 42.
gallic acid, 29.
ipecacuanha, 475.
subsulphate of iron, 102.
opium, 250.
oil of turpentine, 143.
astringent inhalations, 571.
ergot, 599.
Hay fever:
cocaine, 238.
quinine, 83.
Headache:
ammonia, 125.
antacids, 642.
caffeine, 230.
magnesia, 496.
ergot, 600.
Heartburn:
antacids, 641.
Heart-disease:
aconite, 193.
convallaria, 160.
digitalis, 152.
Hoffmann's anodyne, 220.
veratrum viride, 175.
nitrite of amyl, 387.
Hectic fever:
prunus Virginiana, 63.
cold, 716.
Hemiplegia:
strychnine, 335.
electricity, 736.
Hemorrhage from bowels:
tannic acid, 28.
oil of turpentine, 143.
Hemorrhages:
astringents, 28.
oil of erigeron, 546.
oil of eucalyptus, 97.
sulphuric acid, 106.
matico, 552.
subsulphate of iron, 102.
ergot, 599.
acetate of lead, 42.
chlorate of potassium, 542.
Hemorrhoids:
cocaine, 238.
tannic acid, 28.
stramonium, 297.
glycerine, 737.
iodoform, 447.
sulphur, 497.
aloes, 506.
cubebs, 551.
tobacco, 401.
ergotin, 601.
Hepatic abscess:
chloride of ammonium, 576.
escharotics, 619.
Hepatic congestion:
nitric acid, 109.
nitro-muriatic acid, 110.
dandelion, 466.
lemon-juice, 209.
chlorine, 671.
hydragogues, 492.
Hepatic torpor:
potash salts, 535.
wahoo, 508.
Hepatitis:
nitro-muriatic acid, 110.
mercury, 429.
chloride of ammonium, 576.
Hernia:
forced enemata, 490.
Hiccough:
chloral, 375.
musk, 213.
oil of amber, 220.
belladonna, 287.
ether, 315.
Hospital gangrene:
bromine, 624.
Hydrocele:
iodine, 442.
carbolic acid, 684.
Hydrocephalus:
iodide of potassium, 443.
iodoform, 446.
Hydrophobia:
escharotics, 619.
chlorate of potassium, 541.
Hyperemesis:
treatment, 470.
Hyperpyrexia:
quinia, 79.
salicylic acid, 695.
Hypertrophy of heart:
digitalis, 152.
aconite, 193.
Hypertrophy of uterus:
ergot, 601.
Hypochondriasis:
alcohol, 137.
electricity, 741.
Hysteria:
antispasmodics, 212.
bromide of potassium, 362.
bromide of sodium, 366.
brominated camphor, 219.
cocaine, 238.
musk, 213.
valerian, 214.
valerianic acid, 214.
assafetida, 215.
camphor, 218.
conium, 406.
electricity, 740, 741.
anæsthetics, 305.
ether, 315.
oil of wormseed, 649.
oil of amber, 220.
valerianate of ammonium, 214.
Hysterical paralysis:
electricity, 73.

I.

Impotence:
turpentine, 547.
Incontinence of urine:
belladonna, 287.
bromide of iron, 104.
chloral, 375.

- *Incontinence of urine:*
  - strychnine, 336.
  - turpentine, 547.
- *Indigestion:*
  - charcoal, 662.
  - pepsin, 657.
- *Infantile convulsions:*
  - anæsthetics, 305.
  - assafetida, 215.
  - bromide of potassium, 362.
  - brominated camphor, 219.
  - chloral, 375.
  - oil of amber, 220.
  - garlic, 582.
- *Infantile diarrhœa:*
  - phosphate of sodium, 510.
  - thymol, 703.
- *Infantile paralysis:*
  - electricity, 735.
  - strychnine, 336.
- *Inflammations:*
  - borax, 674.
  - lead, 41.
  - blisters, 610.
  - tartar emetic, 167.
  - mercury, 429.
  - cold, 703.
  - stramonium, 297.
  - copaiba, 549.
- *Intermittent fever:*
  - arsenic, 41.
  - apiol, 586.
  - chloroform, 322.
  - chloride of ammonium, 575.
  - eucalyptus, 96.
  - gelsemium, 395.
  - ipecacuanha, 475.
  - hot bath, 553.
  - nitrite of amyl, 388.
  - piperin, 91.
  - quinine, 81.
  - salicylic acid, 696.
- *Intertrigo:*
  - chalk, 647.
- *Intestinal catarrh:*
  - chloride of ammonium, 575.
  - cathartics, 492.
  - eucalyptus, 96.
  - forced enema, 490.
- *Intestinal dyspepsia:*
  - muriatic acid, 107.
  - Calabar bean, 353.
- *Intussusception:*
  - forced enema, 490.
- *Iritis:*
  - atropia, 293.
  - mercury, 429.
- *Irritable heart:*
  - digitalis, 154.
- *Irritative fevers:*
  - aconite, 193.
- *Itch:*
  - sulphur, 497.

J.

- *Jaundice:*
  - emetics, 469.
  - lemon-juice, 210.
  - nitro-muriatic acid, 110.
  - potassium salts, 535.
  - calomel, 502.
  - forced enema, 490.
  - ipecacuanha, 474.
- *Joints, chronic inflammation of:*
  - blisters, 610.
  - cod-liver oil, 451.
  - mercurial plaster, 432.
- *Joints, enlarged:*
  - conium, 406.
  - iodine, 441.
  - cod-liver oil, 451.
  - emplastrum ammoniaci, 577.

K.

- *Keratitis:*
  - atropia, 293.
- *Kidneys, congestion of:*
  - gin, 546.
  - flaxseed, 628.

L.

- *Labor:*
  - anæsthesia, 304.
  - chloroform, 322.
  - ergot, 597.
- *Laryngismus stridulus:*
  - belladonna, 287.
  - chloral, 375.
- *Laryngitis:*
  - gelsemium, 395.
  - glycerine, 737.
  - nitrate of silver, 53.
  - mercury, 429.
  - inhalations, 571.
- *Lead paralysis:*
  - strychnine, 335.
  - electricity, 735.
- *Lead-poisoning:*
  - atropine, 287.
  - alum, 39.
  - sulphuric acid, 105.
  - treatment of, 39.
- *Leucorrhœa:*
  - bismuth, 45.
  - tannic acid, 28.
  - ammonio-ferric alum, 104.
  - iodine, 441.
  - permanganate of potassium, 670.
- *Leukæmia:*
  - ergot, 599.
  - cold, 707.
  - iodoform, 446.
- *Lichen:*
  - arsenic, 419.
- *Locomotor ataxia:*
  - nitrate of silver, 55.
- *Lumbago:*
  - iodide of potassium, 443.
  - cod-liver oil, 452.
  - sulphur, 497.
- *Lupus:*
  - arsenic, 423, 621.
  - phosphorus, 113.
  - mercury, 436.
- *Lymphoma:*
  - arsenic, 418.

M.

- *Malarial neuralgia:*
  - quinine, 82.
- *Malarial poisoning:*
  - chloroform, 322.
  - calomel, 502.
  - gelsemium, 371.
  - quinine, 79, 80.
  - arsenic, 417.
  - epispastics, 609.
  - bebeerine, 60.
  - potassium salts, 535.
  - apiol, 587.
  - ergot, 599.
  - eucalyptus, 96.
  - jaborandi, 564.
  - muriate of ammonia, 575.
  - picric acid, 87.
  - Warburg's tincture, 568.
- *Malignant pustule:*
  - escharotics, 619.
- *Mania:*
  - bromide of potassium, 362.
  - chloral, 373.
  - chloral camphor, 379.
  - croton oil, 519.
  - gelsemium, 395.
  - gamboge, 520.
  - conium, 406.
  - blisters, 610.
- *Mania a potu:*
  - veratrum viride, 174.
  - valerian, 214.
- *Mastitis:*
  - belladonna, 291.
- *Melancholia:*
  - alcohol, 137.
  - cocaine, 238.
- *Meningitis:*
  - cold, 706.
- *Menorrhagia:*
  - aloes, 506.
  - oil of erigeron, 546.
  - acetate of ammonium, 566.
  - rue, 586.
  - savine, 586.
  - ergot, 600.
  - phosphates, 455.

Menstruation, acute suppression of:
 Dover's powder, 558.
 ginger, 91.
 alcohol, 567.
 hot baths, 554.
Mercurial sore mouth:
 tannic acid, 28.
 opium, 251.
 belladonna, 288.
Metallic poisoning:
 iodide of potassium, 443.
Metritis:
 ergot, 600.
Migraine:
 aconite, 195.
 nitrite of amyl, 387.
 muriate of ammonia, 576.
Mitral disease:
 digitalis, 153.
Muscular rheumatism:
 eupatorium, 61.
 ipecacuanha, 475.
 aconite, 193.
 alcohol, 567.
 Dover's powder, 251, 558.
 hot baths, 554.
 iodide of potassium, 443.
 sulphur, 497.
Myelitis:
 electricity, 733.
 nitrate of silver, 55.
 phosphorus, 113.

N.

Narcotic poisoning:
 apomorphine, 480.
 ipecacuanha, 474.
 mustard, 481.
 sulphate of copper, 482.
 sulphate of zinc, 482.
Nasal catarrh:
 eucalyptus, 97.
Nephritis:
 belladonna, 287.
 bitartrate of potassium, 536.
 jaborandi, 564.
Nervous cough:
 belladonna, 287.
 flaxseed, 628.
 gelsemium, 395.
Nervous exhaustion:
 phosphorus, 113.
 Warburg's tincture, 568.
Nervous headache:
 caffeine, 230.
 camphor, 218.
 ether, 315.
 valerianate of ammonium, 214.
Nervous irritability:
 assafetida, 215.
 bromide of potassium, 362.
 prussic acid, 204.
 valerian, 214.
Nervous vomiting:
 hydrocyanic acid, 204.
 carbolic acid, 683.
Neuralgia:
 arsenic, 420.
 bromide of potassium, 362.
 blisters, 610.
 electricity, 737.
 phosphorus, 113.
 veratria, 184.
 aconite, 194.
 alcohol, 137, 138.
 valerianic acid, 214.
 gelsemium, 395.
 cannabis Indica, 267.
 belladonna, 287.
 ether, 315.
 chloral camphor, 379.
 chloroform, 322, 324.
 croton chloral, 380.
 nitroglycerine, 390.
 iodide of potassium, 443.
 iodoform, 446.
 cod-liver oil, 452.
 conium, 406.
 chloride of ammonium, 576.
 valerianate of ammonium, 214.
 quinine, 82.
 ergot, 600.
 epispastics, 610.
Neuralgia, intermittent:
 apiol, 587.
 aromatics, 88.
 arsenic, 418.
 ergot, 601.
 oil of peppermint, 88.
 quinine, 82.
Neuralgia, intestinal:
 alum, 34.
Neuralgia, rheumatic:
 veratrine, 184.
 aconite, 194.
 iodide of potassium, 443.
Neurasthenia:
 cocaine, 238.
Neuritis:
 blister, 610.
Night-pains, syphilitic:
 iodoform, 446.
Night-sweats:
 alum, 33.
 belladonna, 288.
 ergot, 599.
 gallic acid, 29.
 sulphuric acid, 105.
 ipecacuanha, 474.
Nipples, sore:
 tannic acid, 28.
Nymphomania:
 bromide of potassium, 364.

O.

Obstruction of bowels:
 belladonna, 287.
 opium, 250.
Œdema of the lungs:
 jaborandi, 564.
Œsophagus, stricture of:
 anæsthetics, 305.
Onychia maligna:
 nitrate of lead, 43.
 corrosive sublimate, 623.
Ophthalmia:
 iodine, 441.
Opium-poisoning:
 caffeine, 230.
 atropine, 289.
 treatment, 251.
Osmidrosis:
 tannic acid, 28.
Osteomalacia:
 phosphorus, 113.
 phosphates, 455.
Otorrhœa:
 permanganate of potassium, 670.
Ovarian neuralgia:
 gelsemium, 395.
 muriate of ammonia, 576.
Over-secretion:
 astringents, 28.
Oxalic acid diathesis:
 nitric acid, 108.
 nitro-muriatic acid, 110.
Oxyuris vermicularis:
 forced enemata, 490.
Ozæna:
 iodine, 441.
 permanganate of potassium, 670.

P.

Palpitation of heart:
 belladonna, 291.
Paralysis:
 strychnine, 335.
Paralysis agitans:
 conium, 406.
Paraplegia, myelitic:
 nitrate of silver, 55.
 phosphorus, 113.
Parasitic skin-diseases:
 iodine, 441.
 oil of cajeput, 92.
Pemphigus:
 arsenic, 418.
Pericardial effusions:
 iodoform, 446.
 blisters, 611.
 squill, 525.

- *Pericarditis:*
  - mercury, 429.
  - iodide of potassium, 443.
  - iodoform, 446.
- *Periostitis, syphilitic:*
  - phosphates, 455.
- *Peritonitis:*
  - cold, 706.
  - veratrum viride, 170.
  - aconite, 193.
  - opium, 250.
  - mercury, 429.
  - blisters, 610.
  - ipecacuanha, 558.
  - poultices, 636.
- *Pernicious fever:*
  - ammonia, 124.
  - epispastics, 609.
  - mustard, 609.
  - quinine, 81.
- *Phagedænic ulcers:*
  - nitric acid, 108.
- *Phantom tumor:*
  - Calabar bean, 353.
- *Phlegmone:*
  - carbolic acid injections, 684.
- *Phosphatic gravel:*
  - zea mays, 546.
  - benzoic acid, 580.
- *Phosphorus-poisoning:*
  - treatment of, 119.
- *Phthisis:*
  - prunus Virginiana, 63.
  - alcohol, 138.
  - cannabis Indica, 267.
  - conium, 406.
  - eucalyptus, 97.
  - gallic acid, 29.
  - iodine, 441.
  - cod-liver oil, 451.
  - phosphates, 455.
  - strychnine, 336.
  - thymol, 700.
- *Pityriasis:*
  - oil of cajeput, 93.
- *Pleuritic effusion:*
  - iodoform, 446.
  - blisters, 610.
  - squill, 525.
- *Pleuritis:*
  - gelsemium, 395.
  - mercury, 429.
  - jaborandi, 564.
  - iodide of potassium, 443.
  - iodine, 442.
  - blisters, 610.
  - poultices, 636.
- *Pneumonia:*
  - aconite, 193.
  - alcohol, 137.
  - ammonia, 125.
  - belladonna, 288.
  - cold, 703, 713.
  - expectorants, 570.
  - gelsemium, 395.
  - digitalis, 156.
  - oil of turpentine, 143.
- *Pneumonia:*
  - tartar emetic, 167.
  - veratrum viride, 174.
  - musk, 213.
  - chloral, 375.
  - mercury, 429.
  - phosphorus, 113.
  - quinia, 79.
  - blisters, 610.
  - poultices, 636.
  - veratrum viride, 174.
- *Post-partum hemorrhage:*
  - ergot, 598.
  - ipecacuanha, 475.
  - quinia, 75.
- *Pregnancy:*
  - phosphates, 455.
  - confection of senna, 508.
  - ipecacuanha, 474.
- *Priapism:*
  - hops, 221.
- *Prolapsus of the rectum:*
  - emetics, 469.
  - strychnine, 336.
- *Prurigo:*
  - hydrocyanic acid, 204.
- *Pruritus:*
  - chloral camphor, 379.
  - glycerine, 634.
  - tobacco, 401.
- *Psoriasis:*
  - oil of cajeput, 93.
  - phosphorus, 113.
  - chrysophanic acid, 503.
  - arsenic, 419.
  - iodine, 441.
  - glycerine, 634.
- *Psorophthalmia:*
  - yellow oxide of mercury, 436.
- *Pseudo-membranous croup:*
  - alum, 482.
  - ipecacuanha, 474.
  - mercury, 429.
- *Ptyalism:*
  - belladonna, 288.
  - opium, 251.
- *Puerperal convulsions:*
  - nitrite of amyl, 388.
  - anæsthetics, 305.
  - camphor, 218.
  - chloroform, 322.
  - chloral, 374, 375.
  - nitroglycerine, 391.
- *Puerperal fever:*
  - oil of turpentine, 143.
  - digitalis, 156.
  - borax, 675.
- *Puerperal peritonitis:*
  - mercury, 429.
- *Purpura hæmorrhagica:*
  - oil of turpentine, 143.
  - ergot, 599.
- *Pyæmia:*
  - alcohol, 136.
  - tincture of the chloride of iron, 102.
  - quinine, 78.
- *Pyelitis, chronic:*
  - buchu, 543.
  - uva ursi, 544.
  - juniper, 545.
  - turpentine, 547.
  - copaiba, 549.
  - cantharides, 552.
  - salicylic acid, 697.
- *Pyrosis:*
  - bismuth, 45.
  - manganese, 105.
  - nitrate of silver, 54.
  - oxide of silver, 57.

R.

- *Rachitis:*
  - phosphates, 455.
- *Rectum:*
  - feeding by, 659.
- *Relaxation:*
  - astringents, 28.
- *Relaxation of uvula:*
  - pellitory, 605.
- *Remittent fever:*
  - quinia, 82.
  - arsenic, 417.
  - ipecacuanha, 475.
  - Warburg's tincture, 568.
- *Renal calculi:*
  - belladonna, 287.
- *Retention of urine:*
  - strychnine, 336.
- *Retrocedent gout:*
  - ether, 315.
- *Rheumatism:*
  - aconite, 193.
  - arsenic, 420.
  - bromide of ammonium, 366.
  - quinine, 80.
  - jaborandi, 564.
  - conium, 406.
  - cimicifuga, 222.
  - carbolic acid injections, 685.
  - chloroform, 322.
  - oil of amber, 220.
  - oil of cajeput, 93.
  - veratrine, 184.
  - arsenic, 420.
  - iodine, 441.
  - iodide of potassium, 443.
  - iodoform, 446.
  - cod-liver oil, 452.
  - Donovan's solution, 444.
  - Dover's powder, 251, 558.
  - colchicum, 461.
  - guaiac, 465.
  - hot baths, 556.
  - opium, 251.
  - magnesia, 496.
  - mercury, 436.
  - nitrate of potassium, 538.

Rheumatism :
- sulphur, 497.
- Scudamore's mixture, 461.
- alcohol, 567.
- Burgundy pitch, 618.
- pellitory, 605.
- sulphurated potassa, 497.

Rheumatism, inflammatory :
- quinia, 79, 80.
- lemon-juice, 209.
- cimicifuga, 222.
- benzoic acid, 580.
- bromide of ammonium, 366.
- iodide of potassium, 443.
- potassium salts, 535.
- nitrate of potassium, 538.
- salicin, 698.
- salicylic acid, 696.
- Dover's powder, 558.
- vinegar, 210.

Rheumatoid arthritis :
- arsenic, 420.
- iodide of potassium, 443.

Rhus toxicodendron poisoning :
- lobelia, 391.

Rickets :
- phosphorus, 113.
- cod-liver oil, 451.

Rigidity of os uteri :
- belladonna, 287.

Round worms :
- oil of turpentine, 142, 654.
- spigelia, 649.
- azedarach, 649.
- chenopodium, 649.
- santonin, 653.
- mucuna, 655.

S.

Scabies :
- glycerine, 634.

Scarlet fever :
- aconite, 193.
- belladonna, 288, 294.
- cold, 706, 715.
- chlorate of potassium, 541.
- quinine, 79.

Sciatica :
- conium, 406.
- iodide of potassium, 443.
- cod-liver oil, 452.
- sulphur, 497.
- electricity, 737.

Scrofulosis :
- alcohol, 138.
- sarsaparilla, 464.
- pipsissewa, 515.
- iodine, 441.
- cod-liver oil, 451.
- phosphoric acid, 455.
- phosphates, 455.
- syrup of iodide of iron, 103.

Scrofulous tumors :
- emplastrum ammoniaci, 577.

Scrofulous ulcers :
- sulphurated lime, 498.

Scurvy :
- lemon-juice, 209.
- chlorate of potassium, 541.
- vinegar, 210.

Seat-worms :
- forced enemata, 490.
- quassia, 59.
- oil of cajeput, 92.
- vinegar, 210.

Seborrhœa :
- glycerine, 634.

Septicæmia :
- quinia, 79.
- borax, 675.

Sexual excitement :
- bromide of potassium, 362.
- camphor, 218.
- hops, 221.

Shock :
- epispastics, 609.
- hot baths, 705.

Sick headache :
- antacids, 642.
- magnesia, 496.

Sick stomach :
- ipecacuanha, 474.

Singultus :
- chloral, 375.

Sinking spells :
- ether, 315.

Skin, affections of :
- arsenic, 418.
- chalk, 647.
- cod-liver oil, 452.
- Donovan's solution, 444.
- magnesia, 496.
- nitro-muriatic acid, 110.
- tar, 583.
- oxide of mercury, 436.
- copaiba, 550.
- oxide of zinc, 46.
- sulphur, 497.
- sulphurated potassa, 498.

Sleeplessness :
- opium, 249.
- chloral, 373.
- bromide of potassium, 362.
- hyoscine, 301.

Smallpox :
- opium, 250.

Snake-poisoning :
- ammonia, 124.
- alcohol, 136.

Softening of brain :
- phosphorus, 113.

Sore throat :
- tannic acid, 28.
- alum, 33.
- chlorine water, 671.
- nitrate of silver, 53.
- belladonna, 287.
- chlorate of potassium, 542.
- sumach berries, 542.
- gum arabic, 625.
- carbolic acid, 683.

Spasms :
- atropia, 287.
- opium, 249.
- assafetida, 215.
- oil of cajeput, 92.
- aconite, 193.
- belladonna, 287.
- anæsthetics, 304.

Spermatorrhœa :
- brominated camphor, 219.
- chloral, 375.
- turpentine, 547.

Spinal anæmia or irritation :
- electricity, 740.

Spinal congestion :
- electricity, 740.
- ergot, 600.

Spinal depression :
- strychnine, 335.

Spleen, enlargement of :
- bromide of potassium, 364.
- cold, 706.
- ergot, 599.

Spongy gums :
- tannic acid, 28.

Sprains :
- camphor, 218.
- Goulard's extract, 41.
- vinegar, 210.

Status epilepticus :
- nitrite of amyl, 388.

Stomatitis :
- chlorate of potassium, 541.
- carbolic acid, 683.
- thymol, 703.

Strangury :
- opium, 254.

Stricture, spasmodic.
- belladonna, 287.
- anæsthetics, 305.

Strychnia-poisoning :
- treatment, 340.
- Calabar bean, 352.
- bromide of potassium. 363, 374.
- chloral, 375.
- nitrite of amyl, 340, 389.
- tobacco, 400.

Subinvolution of uterus :
- ergot, 601.

Sunburn :
- vinegar, 210.

Suppressed menstruation :
ginger, 91.
Dover's powder, 558.
alcohol, 567.
Suppression of urine :
digitalis, 526.
Sweating, excessive :
gallic acid, 29.
chalk, 647.
jaborandi, 564.
Syncope :
ammonia, 124.
alcohol, 136.
digitalis, 155.
ether, 315.
nitrite of amyl, 388.
Synovitis, chronic :
carbolic acid injections, 685.
Syphilis :
nitric acid, 108.
nitro-muriatic acid, 110.
mercury, 429, 436.
iodide of potassium, 443.
iodoform, 446.
cod-liver oil, 451.
sarsaparilla, 464.
guaiac, 465.
chlorate of potassium, 541.
phosphates, 455.
Syphilitic nodes :
emplastrum ammoniaci cum hydrargyro, 577.

T.

Tabes mesenterica :
cod-liver oil, 451.
Tape-worm :
ether, 315.
forced enemata, 490.
chenopodium, 650.
brayera, 650.
pepo, 654.
picric acid, 87.
rottlera, 655.
male fern, 654.
mucuna, 655.
pomegranate, 655.
turpentine, 654.
Teething :
brominated camphor, 219.
Tetanus :
cannabis Indica, 267.
Calabar bean, 352.
bromide of potassium, 362.
chloral, 374.
lobelia, 392.
nitrite of amyl, 388.
tobacco, 400.
Tic douloureux :
croton chloral, 381.
gelsemium, 395.
Tinea capitis :
lime-water, 646.
Tonsillitis :
tincture of capsicum, 92.
Toothache :
chloral camphor, 379.
oil of cloves, 90.
pellitory, 605.
Trichiniasis :
picric acid, 87.
Trismus nascentium :
Calabar bean, 352.
chloral, 375.
Tuberculosis :
cod-liver oil, 452.
Tympanitis :
assafetida, 215.
Typhoid fever :
quinia, 79.
alcohol, 136.
cold, 707.
jaborandi, 564.
oil of turpentine, 142.
digitalis, 156.
veratrum viride, 174.
salicylic acid, 695.
mineral acids, 107.
thymol, 700.
antipyrin, 703.
Typhus fever :
alcohol, 136.
belladonna, 288.
chloral, 373.
chlorine water, 671.
cold, 710.
salicylic acid, 695.
digitalis, 156.
quinia, 79.

U.

Ulcer of cervix uteri :
solution of nitrate of mercury, 623.
Ulcer of cornea :
atropia, 293.
Ulceration, chronic :
conium, 406.
iodoform, 446.
Ulceration of bowels :
oil of turpentine, 142.
Ulcers :
alum, 33.
bismuth, 45.
borax, 674.
carbolic acid, 685.
chloride of zinc, 622.
conium, 406.
chloral, 376.
chalk, 647.
charcoal, 662.
escharotics, 623.
iodoform, 446.
nitrate of silver, 53.
nitric acid, 108.
sulphuric acid, 105.
sulphate of copper, 47.
tannic acid, 28.
lime-water, 646.
chlorine water, 671.
Ulcers :
cold, 706.
permanganate of potassium, 670.
Unilateral sweating :
jaborandi, 564.
Ununited fracture :
phosphates, 455.
Uræmia :
chloral, 376.
opium, 251.
elaterium, 517.
jaborandi, 564.
nitroglycerine, 390.
Uræmic convulsions :
chloral, 374.
Urethral fever :
aconite, 193.
bromide of potassium, 362.
Urethral spasm :
belladonna, 287.
Urethritis :
nitrate of silver, 54.
Uric acid calculus and gravel :
benzoic acid, 580.
potassium salts, 535.
soda salts, 645.
zea mays, 546.
Uric acid diathesis :
benzoic acid, 580.
carbonate of lithium, 542.
potassium salts, 532.
sodium salts, 645.
Urticaria :
arsenic, 419.
emetics, 469.
Uterine inertia :
ergot, 597.
smut of Indian corn, 604.
Uterus, cancer of :
Chian turpentine, 143.
chloral, 376.
iodoform, 447.
Uterus, subinvolution of :
ergot, 601.
Uvula, relaxation of :
pellitory, 605.

V.

Valvular disease of heart :
digitalis, 152.
aconite, 193.
veratrum viride, 175.
compound spirit of ether, 220.
Venereal ulcers :
Canquoin's paste in, 622.
Venereal warts :
nitric acid, 108.
Veratrum viride poisoning :
treatment, 175.
Vesical catarrh :
benzoic acid, 580.

Vomiting:
  bismuth, 45.
  ipecacuanha, 474.
  prussic acid, 204.
  opium, 250, 254.
  oxalate of cerium, 45.
  lime-water, 645.
  carbolic acid, 683.
Vomiting, excessive:
  treatment of, 470.
Vomiting of pregnancy:
  aconite, 194.
  bromide of potassium, 362.
  ipecacuanha, 474.
  oxalate of cerium, 45.

W.

White swelling:
  cod-liver oil, 451.
Whooping-cough:
  assafetida, 215.
  camphor, 218.
  belladonna, 287.
  hyoscine, 300.
  gelsemium, 395.
  bromide of ammonium, 366.
  chloral, 375.
  conium, 406.
  arsenic, 420.
  lobelia, 392.
  quinine, 83.
  ergot, 600.
  oil of amber, 220.
Winter cough:
  strychnine, 336.
Wounds:
  alcohol dressing, 139.
  carbolic acid, 684.
  salicylic acid, 697.
  carbolated camphor, 219.
  charcoal, 662.

THE END.